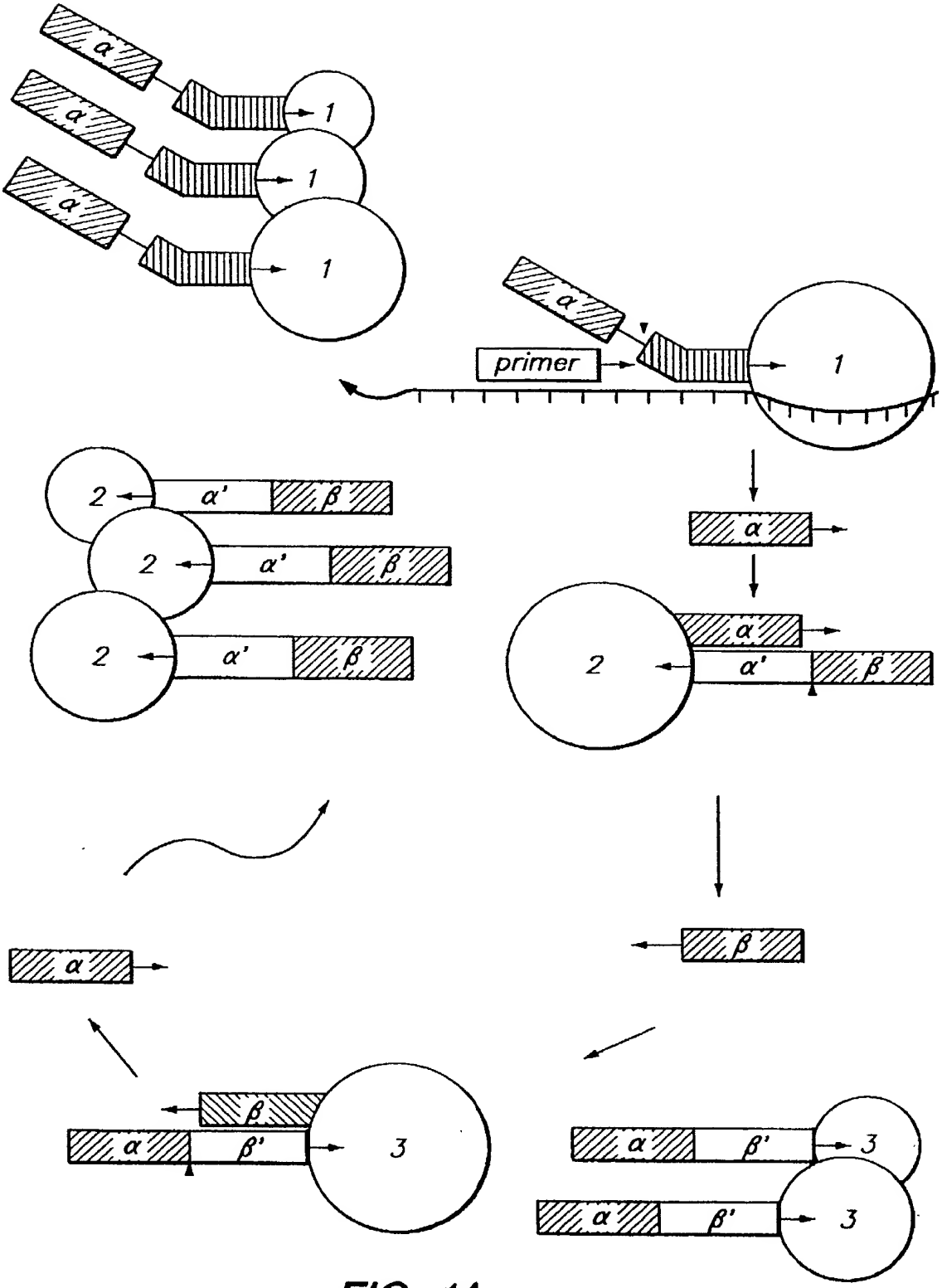


FIG. 1A

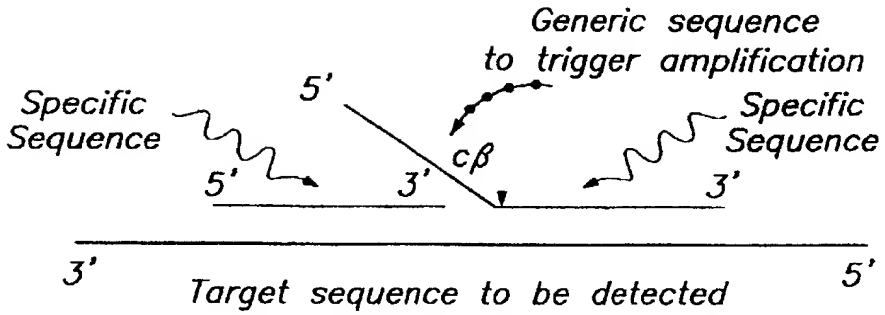


FIG. 1B PART ONE: TRIGGER REACTION

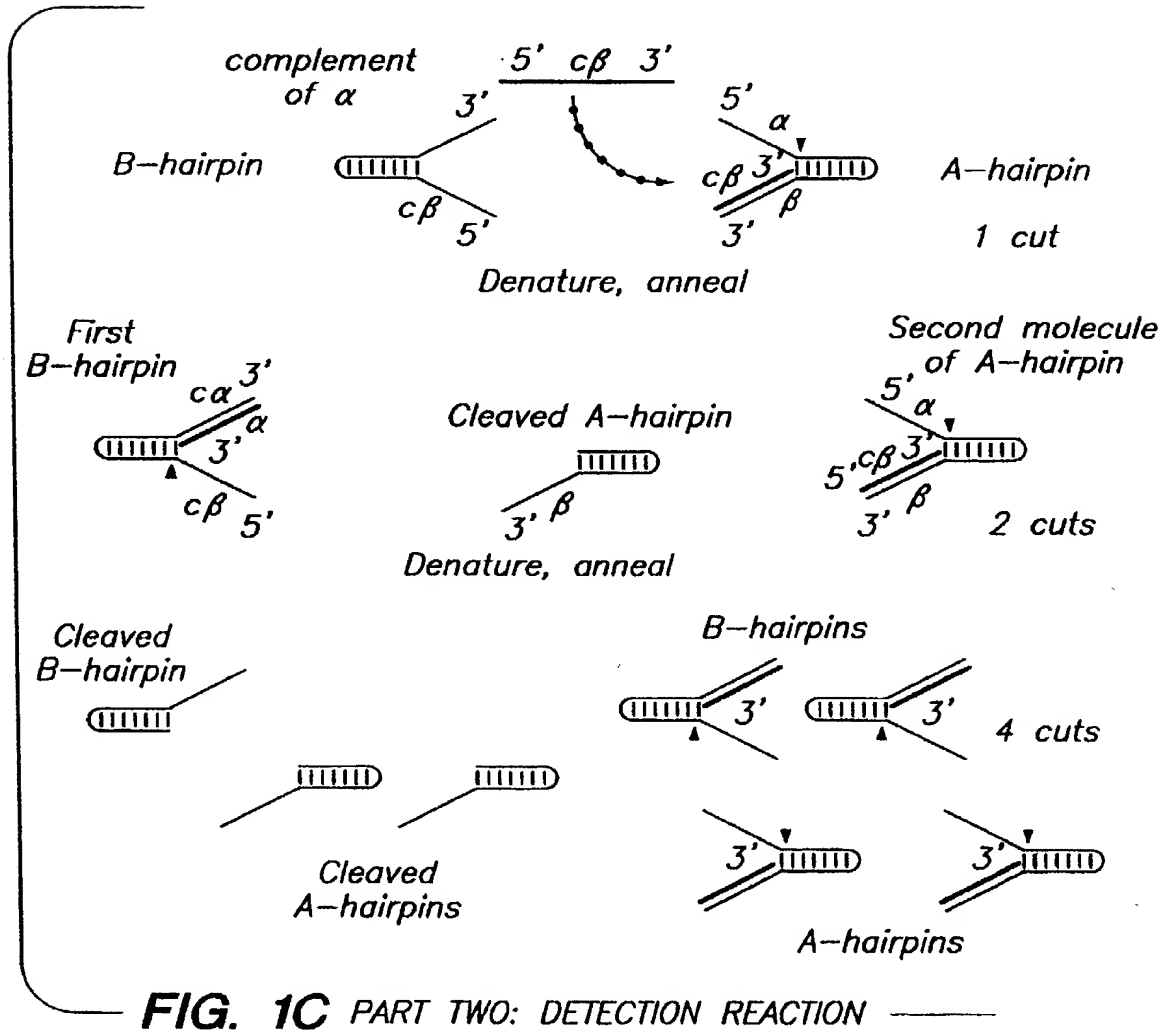


FIG. 1C PART TWO: DETECTION REACTION

FIG. 2A

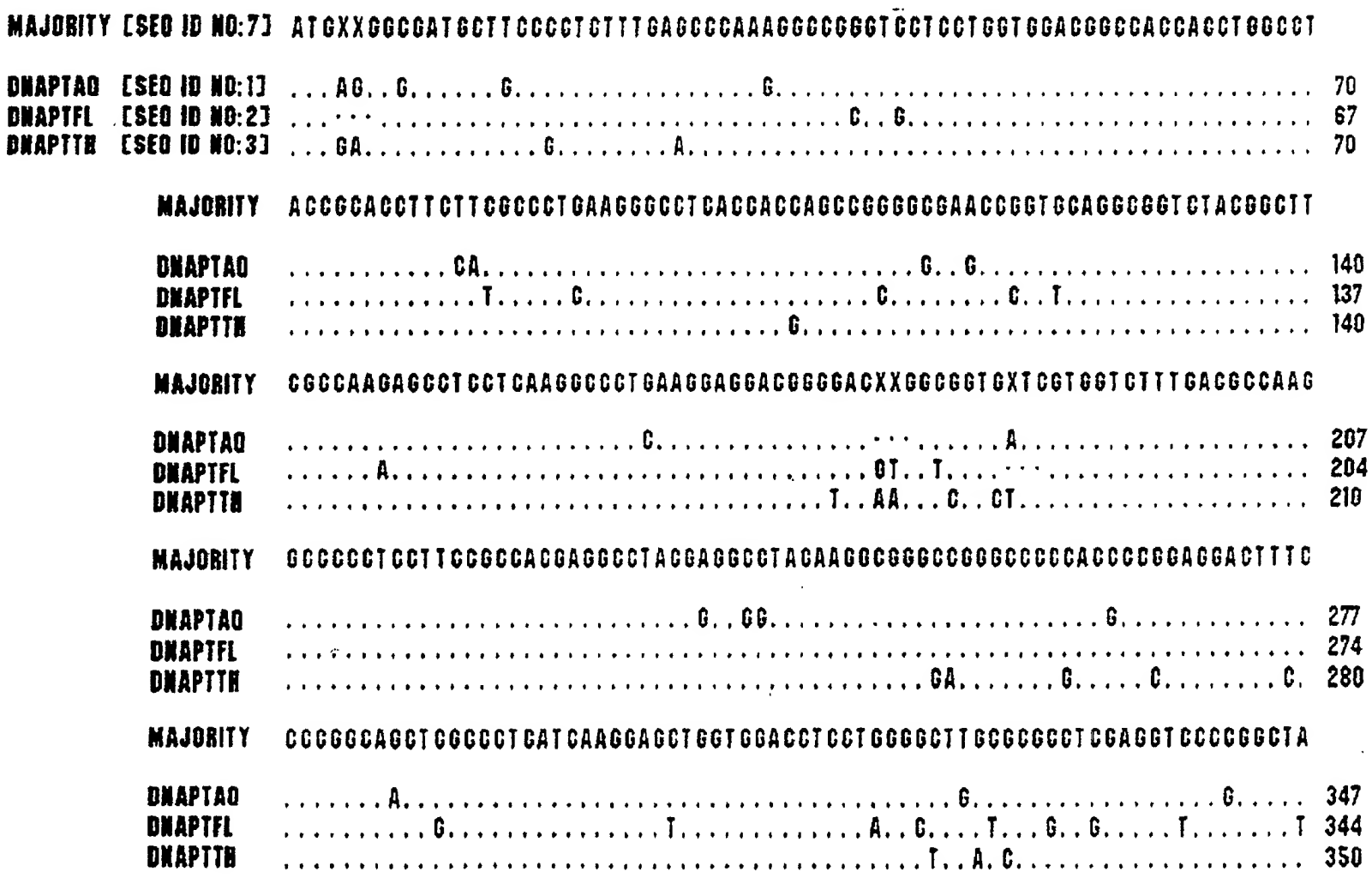

MAJORITY [SEQ ID NO:7] ATGXXGGCGATGCTTCCCCTCTTTGAGCCCAAAGGCCGGGTCCTCCTGGTGGACGGCCACCACCTGGCCT
DNAPTAQ [SEQ ID NO:1] ...AG..G.....G.....G..... 70
DNAPTFL [SEQ ID NO:2] .....C..G..... 67
DNAPTTH [SEQ ID NO:3] ...GA.....G.....A..... 70
MAJORITY ACCGCACCTTCTTCGCCCTGAAGGCCTCACCACCAGCCGGGGCGAACCGGTGCAGGCGGTCTACGGCTT
DNAPTAQ .....CA.....G..G..... 140
DNAPTFL .....T.....C.....C.....C..T..... 137
DNAPTTH .....G..... 140
MAJORITY CGCCAAGAGCCTCCTCAAGCCCCTGAAGGAGGACGGGGACXXGGCGGTGXTCGTGGTCTTTGACGCCAAG
DNAPTAQ .....C.....A..... 207
DNAPTFL .....A.....GT..T..... 204
DNAPTTH .....T..AA...C..CT..... 210
MAJORITY GCCCCCTCCTTCCGCCACGAGGCCTACGAGGCCTACAAGGCGGGCCGGGCCCCCACCCCGGAGGACTTTC
DNAPTAQ .....G..GG.....G..... 277
DNAPTFL 274
DNAPTTH .....GA.....G.....C.....C. 280
MAJORITY CCCGGCAGCTCGCCCTCATCAAGGAGCTGGTGGACCTCCTGGGGCTTGCGCGCCTCGAGGTCCCCGGCTA
DNAPTAQ .....A.....G.....G..... 347
DNAPTFL .....G.....T.....A..C....T...G..G.....T.....T 344
DNAPTTH .....T..A.C..... 350

FIG. 2B

```
MAJORITY [SEQ ID NO:7] CGAGGCGGACGACGTXGTGGCCACCCTGGCCAAGAAGGCGGAAAAGGAGGGGTACGAGGTGCGCATCCTC

DNAPTAQ  [SEQ ID NO:1] ..............C.......G.............................C........C.........  417
DNAPTFL  [SEQ ID NO:2] T.............G.................CG.....................................  414
DNAPTTH  [SEQ ID NO:3] ..............T..C.....................................................  420

MAJORITY ACCGCCGACCGCGACCTCTACCAGCTCCTTTCCGACCGCATCGGCGTCCTCCACCCCGAGGGGTACCTCA

DNAPTAQ  .........AAA.....T.........................CA.............................  487
DNAPTFL  ..T.............................G..G.........A..........T...........G.  484
DNAPTTH  ........................A...G.C.........G.....................CC.......  490

MAJORITY TCACCCCGGCGTGGCTTTGGGAGAAGTACGGCCTGAGGCCGGAGCAGTGGGTGGACTACCGGGCCCTGGC

DNAPTAQ  ..........C...........A.................C..C.......CC...............A.  557
DNAPTFL  ...................AC..............C.C.................................  554
DNAPTTH  .........A.........................C.....................T...C.....C.T  560

MAJORITY GGGGGACCCCTCCGACAACCTCCCCGGGGTCAAGGGCATCGGGGAGAAGACCGCCCXGAAGCTCCTCXAG

DNAPTAQ  C......GAG...........T.............................G..GAG......T..GG..  627
DNAPTFL  ............G..T...A.........G.........................A..G....A..CGC  624
DNAPTTH  ..................................................TC.........A..        630

MAJORITY GAGTGGGGGAGCCTGGAAAACCTCCTCAAGAACCTGGACCGGGTGAAGCCCGC···CXTCCGGGAGAAGA

DNAPTAQ  ..................GC.......................C.............A.............  694
DNAPTFL  .........................T..C..C.........A..........T.···.T.G.........C  691
DNAPTTH  ........A.....................................A.....A.AAAA.G.............  700
```

FIG. 2C

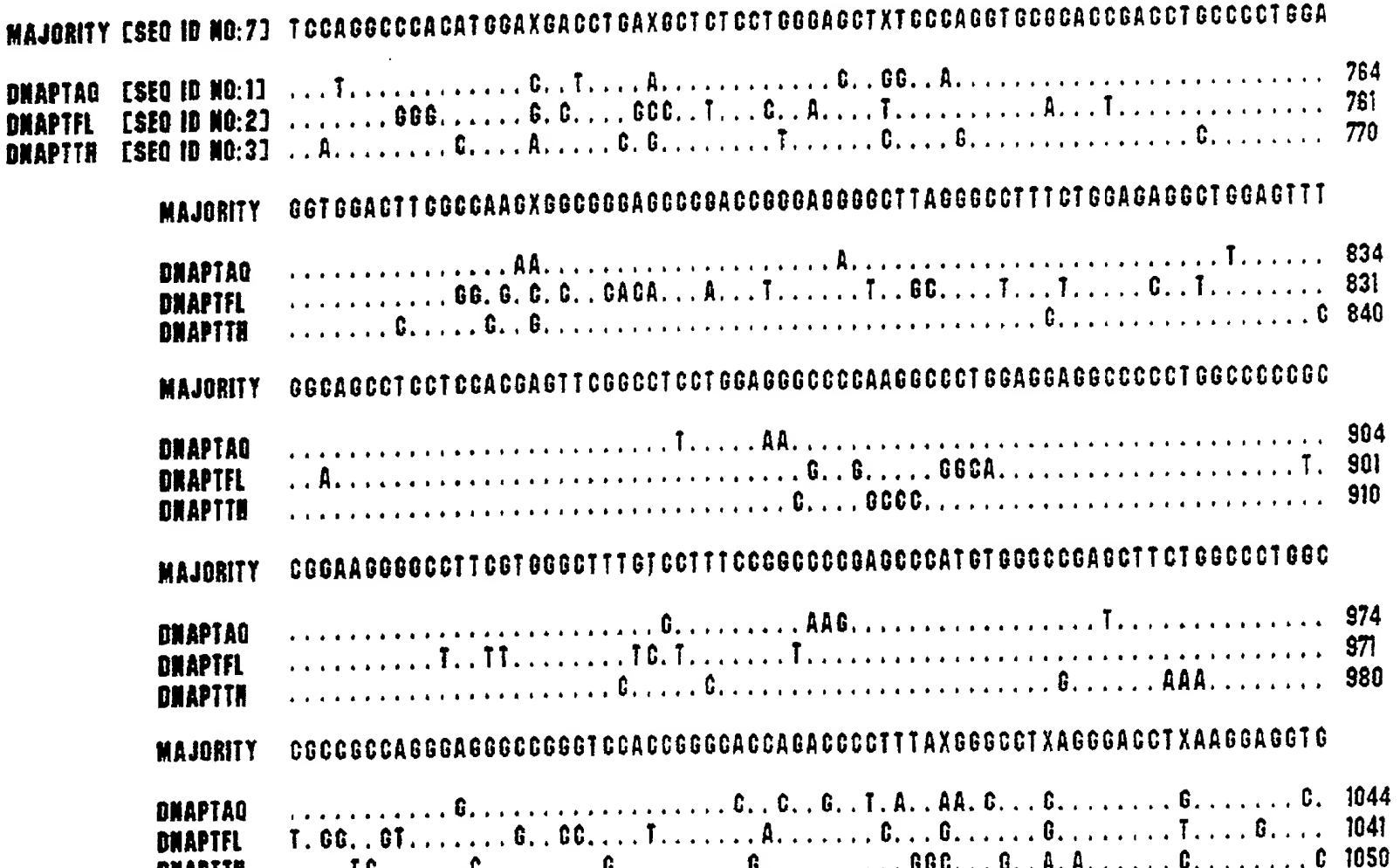

MAJORITY [SEQ ID NO:7] TCCAGGCCCACATGGAXGACCTGAXGCTCTCCTGGGAGCTXTCCCAGGTGCGCACCGACCTGCCCCTGGA
DNAPTAQ [SEQ ID NO:1] ...T.....C..T....A.....C..GG..A..... 764
DNAPTFL [SEQ ID NO:2] .....GGG.....G.C....GCC..T...C..A....T.....A...T..... 761
DNAPTTH [SEQ ID NO:3] ..A.....C....A.....C.G.....T.....C....G.....C..... 770
MAJORITY GGTGGACTTCGCCAAGXGGCGGGAGCCCGACCGGGAGGGGCTTAGGGCCTTTCTGGAGAGGCTGGAGTTT
DNAPTAQ .....AA.....A.....T..... 834
DNAPTFL .....GG.G.C.C..CAGA...A...T.....T..GC....T...T.....C..T..... 831
DNAPTTH .....C.....C..G.....G.....C 840
MAJORITY GGCAGCCTCCTCCACGAGTTCGGCCTCCTGGAGGGCCCCAAGGCCCTGGAGGAGGCCCCCTGGCCCCCGC
DNAPTAQ .....T.....AA..... 904
DNAPTFL ..A.....G..G.....GGCA.....T. 901
DNAPTTH .....C....GCCC..... 910
MAJORITY CGGAAGGGGCCTTCGTGGCTTTGTCCTTTCCGGCCCGAGCCCATGTGGGCCGAGCTTCTGGCCCTGGC
DNAPTAQ .....G.....AAG.....T..... 974
DNAPTFL .....T..TT.....TC.T.....T..... 971
DNAPTTH .....C.....C.....G.....AAA..... 980
MAJORITY CGCCGCCAGGGAGGGCCGGGTCCACCGGGGACCAGACCCCTTTAXGGGCCTXAGGGACCTXAAGGAGGTG
DNAPTAQ .....G.....C..C..G..T.A..AA.C...C.....G.....C. 1044
DNAPTFL T.GG..GT.....G..CC....T.....A.....C...G.....G.....T....G.... 1041
DNAPTTH ....TG.....C.....G.....G.....GGC...G..A.A.....C.....C 1050

FIG. 2D

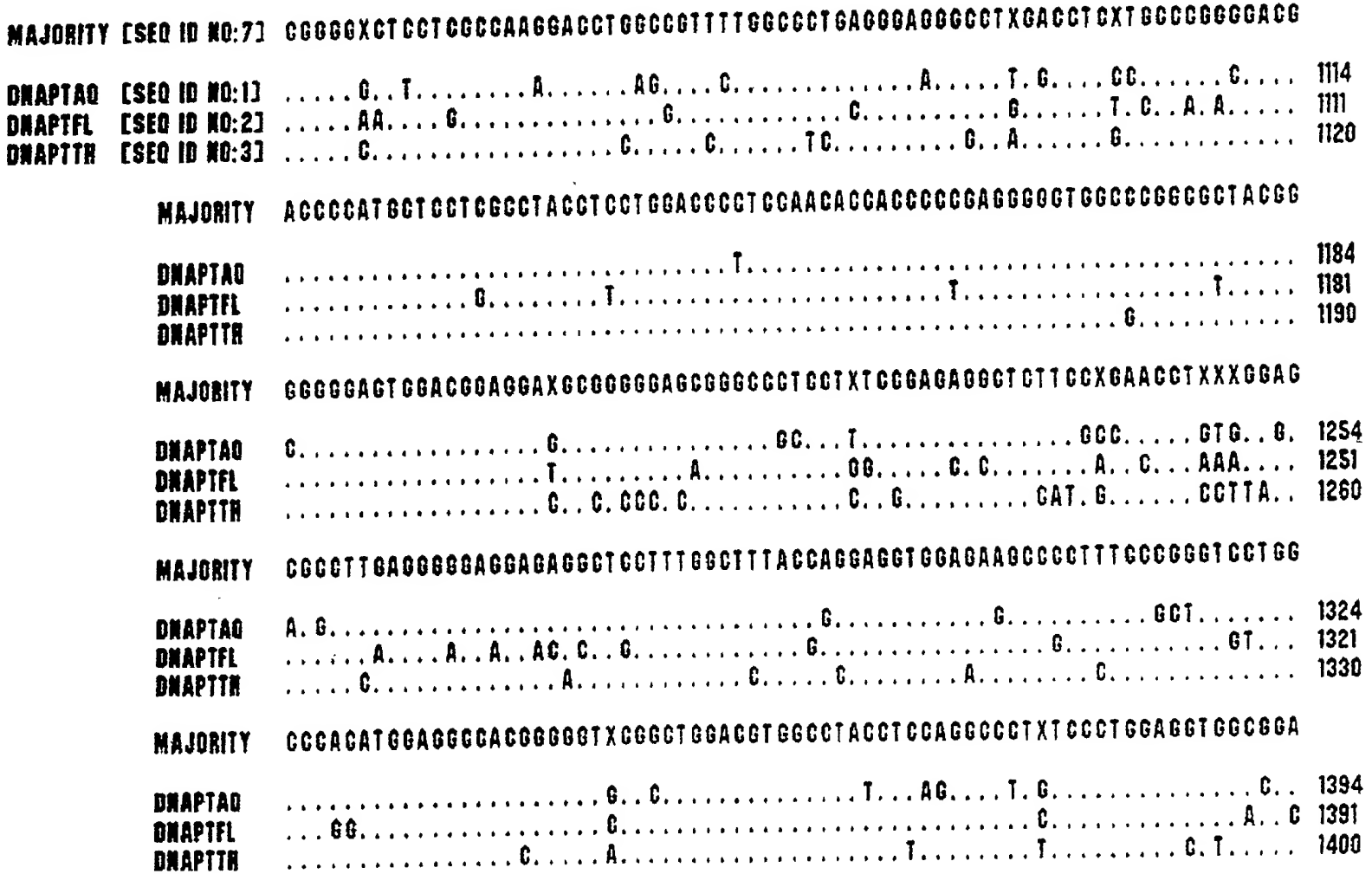

MAJORITY [SEQ ID NO:7] GGGGGXCTCCTCGCCAAGGACCTGGCCGTTTTGGCCCTGAGGGAGGGCCTXGACCTCXTGCCCGGGGACG
DNAPTAQ [SEQ ID NO:1] .....G..T.....A.....AG....C.....A.....T.G....CC.....C.... 1114
DNAPTFL [SEQ ID NO:2] .....AA....G.....G.....C.....G.....T.C..A.A..... 1111
DNAPTTR [SEQ ID NO:3] .....C.....C.....C.....TC.....G..A.....G..... 1120
MAJORITY ACCCCATGCTCCTCGCCTACCTCCTGGACCCCTCCAACACCACCCCCGAGGGGCTGGCCCGGCGCTACGG
DNAPTAQ .....T..... 1184
DNAPTFL .....G.....T.....T.....T..... 1181
DNAPTTR .....G..... 1190
MAJORITY GGGGGAGTGGACGGAGGAXGCGGGGGAGCGGGCCCTCCTXTCGGAGAGGCTCTTCCXGAACCTXXXGGAG
DNAPTAQ C.....G.....GC...T.....GCC.....GTG..G. 1254
DNAPTFL .....T.....A.....GG.....C.C.....A..C...AAA.... 1251
DNAPTTR .....C..C.CCC.C.....C..G.....CAT.G.....CCTTA.. 1260
MAJORITY CGCCTTGAGGGGGAGGAGAGGCTCCTTTGGCTTTACCAGGAGGTGGAGAAGCCCCTTTCCCGGGTCCTGG
DNAPTAQ A.G.....G.....G.....GCT..... 1324
DNAPTFL .....A....A..A..AC.C..G.....G.....G.....GT... 1321
DNAPTTR .....C.....A.....C.....C.....A.....C..... 1330
MAJORITY CCCACATGGAGGGCACGGGGGTXCGGCTGGACGTGGCCTACCTCCAGGCCCTXTCCCTGGAGGTGGCGGA
DNAPTAQ .....G..C.....T...AG....T.G.....C.. 1394
DNAPTFL ...GG.....C.....C.....A..C 1391
DNAPTTR .....C.....A.....T.....T.....C.T..... 1400

FIG. 2E

```
MAJORITY [SEQ ID NO:7] GGAGATCCGGCCGCCTCGAGGAGGAGGTCTTCCGCCTGGCCGGCCACCCCTTCAACCTCAACTCCCGGGAC

DNAPTAQ  [SEQ ID NO:1] .......GC..........CC................................................ 1464
DNAPTFL  [SEQ ID NO:2] ....G.G....AG..G...................................................C.. 1461
DNAPTTH  [SEQ ID NO:3] ..................................T....G.............................. 1470

MAJORITY               CAGCTGGAAAGGGTGCTCTTTGACGAGCTXGGGCTTCCCGCCATCGGCAAGACGGAGAAGACXGGCAAGC

DNAPTAQ                ..............C..............A................................C....... 1534
DNAPTFL                ........GC...................G..C..G..T.......................G..G..A. 1531
DNAPTTH                .............................TA...........T.G..G......C.A.....A....... 1540

MAJORITY               GCTCCACCAGCGCCGCCGTGCTGGAGGCCCTXCGXGAGGCCCACCCCATCGTGGAGAAGATCCTGCAGTA

DNAPTAQ                ...................C...........C..C................................... 1604
DNAPTFL                .............T.................G..A....................CCGC........... 1601
DNAPTTH                ................G..............A..G.............................C...C. 1610

MAJORITY               CCGGGAGCTCACCAAGCTCAAGAACACCTACATXGACCCCCTGCCXGXCCTCGTCCACCCCAGGACGGGC

DNAPTAQ                ..................G....G.........T......T....G.A....A................. 1674
DNAPTFL                .................................A...........C.C...G..........A...C... 1671
DNAPTTH                ...............................G.G........C..AAG............G......... 1680

MAJORITY               CGCCTCCACACCCGCTTCAACCAGACGGCCACGGCCACGGGCAGGCTTAGTAGCTCCGACCCCAACCTGC

DNAPTAQ                ...............................................A...........T........C. 1744
DNAPTFL                ..G.............................C...............TCC................... 1741
DNAPTTH                .........................................G............................ 1750
```

FIG. 2F

```
MAJORITY [SEQ ID NO:7] AGAACATCCCCGTCCGCACCCCXCTGGGCCAGAGGATCCGCCGGGCCTTCGTGGCCGAGGAGGGXTGGGT

DNAPTAQ  [SEQ ID NO:1] .....G..T..G.....A.C.....G...C. 1814
DNAPTFL  [SEQ ID NO:2] .....G.....T.....C.C.....A.....C..... 1811
DNAPTTH  [SEQ ID NO:3] .....CT.....C...T....C 1820

MAJORITY GTTGGTGGCCCTGGACTATAGCCAGATAGAGCTCCGGGTCCTGGCCCACCTCTCCGGGGACGAGAACCTG

DNAPTAQ  A.....A....G.....C..... 1884
DNAPTFL  .C.....T.T.....C.....T....T..... 1881
DNAPTTH  .....C.....C.....A..... 1890

MAJORITY ATCCGGGTCTTCCAGGAGGGGAGGGACATCCACACCCAGACGGCCAGCTGGATGTTCGGCGTCCCCCCGG

DNAPTAQ  .....C.....GG.....G.. 1954
DNAPTFL  .....T.....TT....C. 1951
DNAPTTH  ...A.....A.....A..... 1960

MAJORITY AGGCCGTGGACCCCCTGATGCGCCGGGCGGCCAAGACCATCAACTTCGGGGTCCTCTACGGCATGTCGGC

DNAPTAQ  .....G.. 2024
DNAPTFL  .A.GG..A.....T.....G..... 2021
DNAPTTH  .....GG.G.....C..... 2030

MAJORITY CCACCGCCTCTCCCAGGAGCTTGCCATCCCCTACGAGGAGGCGGTGGCCTTCATTGAGCGCTACTTCCAG

DNAPTAQ  .....A.....T.....CCA.....T... 2094
DNAPTFL  .....GG.....T..... 2091
DNAPTTH  ...TA.G.....T..A.....A 2100
```

FIG. 2G

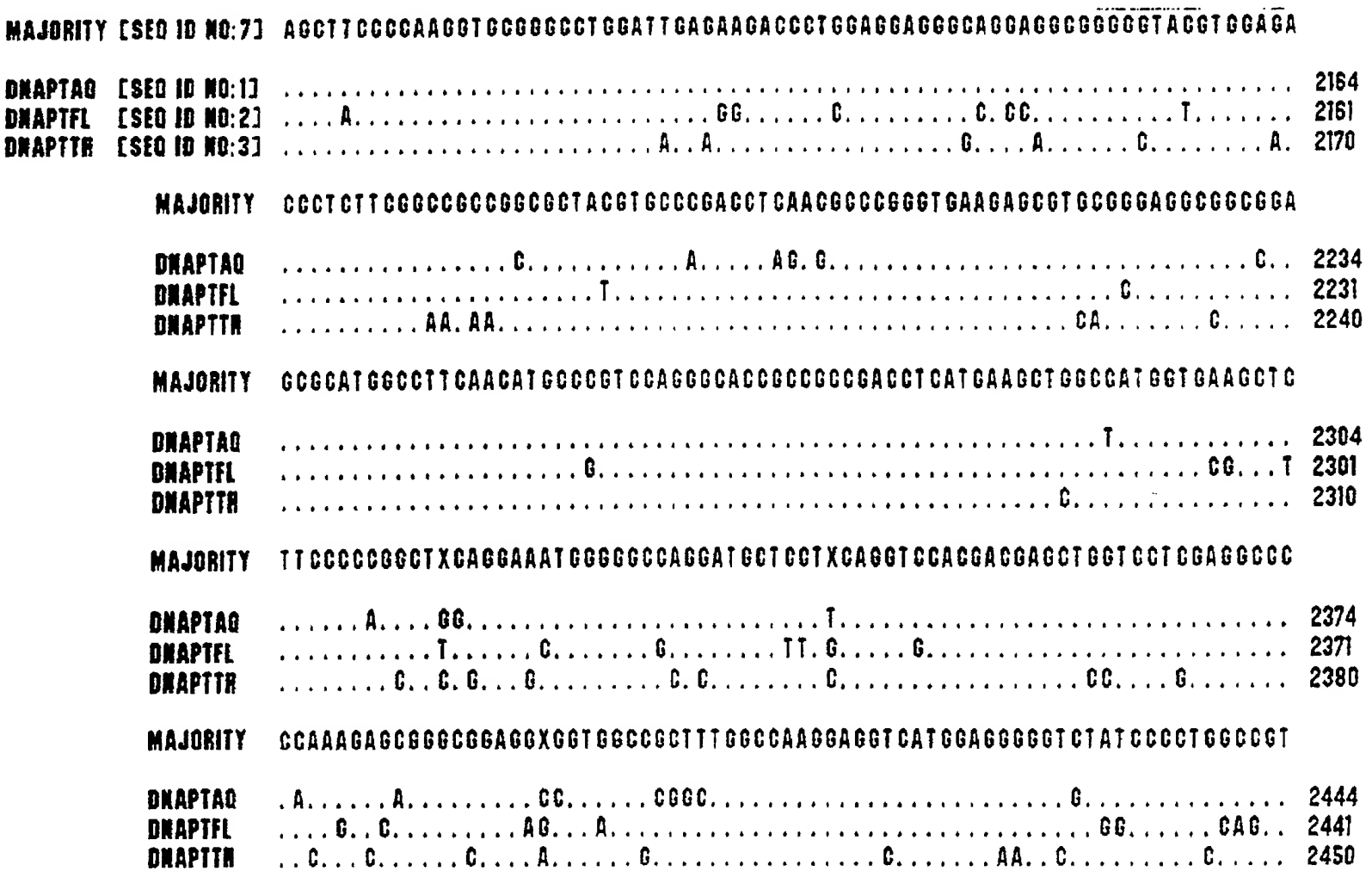

MAJORITY [SEQ ID NO:7] AGCTTCCCCAAGGTGCGGGCCTGGATTGAGAAGACCCTGGAGGAGGGCAGGAGGCGGGGGTACGTGGAGA
DNAPTAQ [SEQ ID NO:1] 2164
DNAPTFL [SEQ ID NO:2] ....A.....GG.....C.....C.CC.....T..... 2161
DNAPTTR [SEQ ID NO:3] .....A..A.....G....A.....C.....A. 2170
MAJORITY CCCTCTTCGGCCGCCGGCGCTACGTGCCCGACCTCAACGCCCGGGTGAAGAGCGTGCGGGAGGCGGCGGA
DNAPTAQ .....C.....A.....AG.G.....C.. 2234
DNAPTFL .....T.....C..... 2231
DNAPTTR .....AA.AA.....CA.....C..... 2240
MAJORITY GCGCATGGCCTTCAACATGCCCGTCCAGGGCACCGCCGCCGACCTCATGAAGCTGGCCATGGTGAAGCTC
DNAPTAQ .....T..... 2304
DNAPTFL .....G.....CG...T 2301
DNAPTTR .....C..... 2310
MAJORITY TTCCCCCGGCTXCAGGAAATGGGGGCCAGGATGCTCGTXCAGGTCCACGACGAGCTGGTCCTCGAGGCCC
DNAPTAQ .....A....GG.....T..... 2374
DNAPTFL .....T.....C.....G.....TT.G.....G..... 2371
DNAPTTR .....C..C.G...G.....C.C.....C.....CC....G..... 2380
MAJORITY CCAAAGAGCGGGCGGAGGXGGTGGCCGCTTTGGCCAAGGAGGTCATGGAGGGGGTCTATCCCCTGGCCGT
DNAPTAQ .A.....A.....CC.....CGGC.....G..... 2444
DNAPTFL ....G..C.....AG...A.....GG.....CAG.. 2441
DNAPTTR ..C...C.....C....A.....G.....C.....AA..C.....C..... 2450

FIG. 2H

```
MAJORITY [SEQ ID NO:7] GCCCCTGGAGGTGGAGGTGGGGATGGGGGAGGACTGGCTCTCCGCCAAGGAGTAG

DNAPTAQ  [SEQ ID NO:1] .........................A.............................GA 2499
DNAPTFL  [SEQ ID NO:2] .....................CC.................................. 2496
DNAPTTH  [SEQ ID NO:3] ...................................T.........GT... 2505
```

FIG. 3A

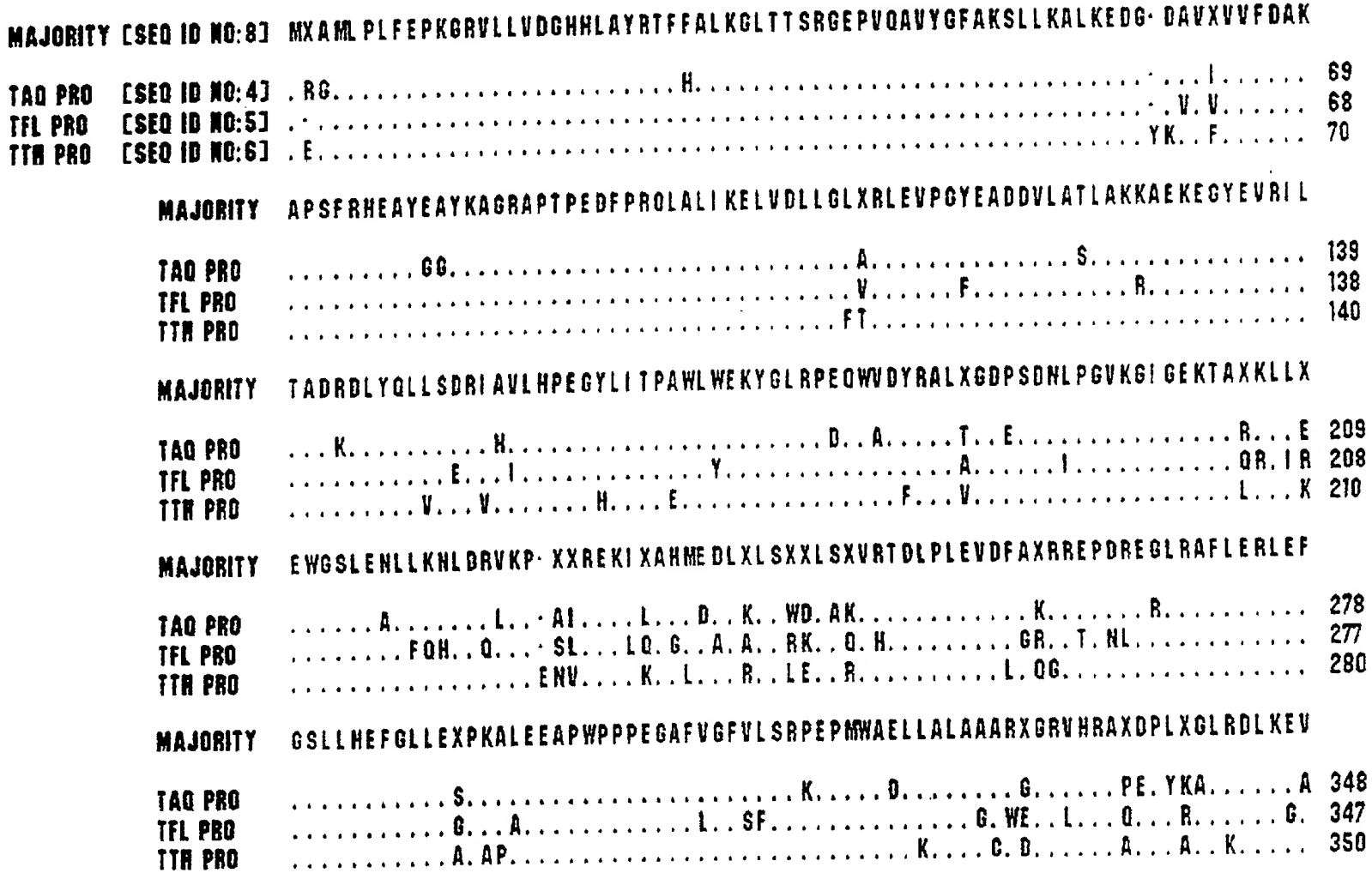
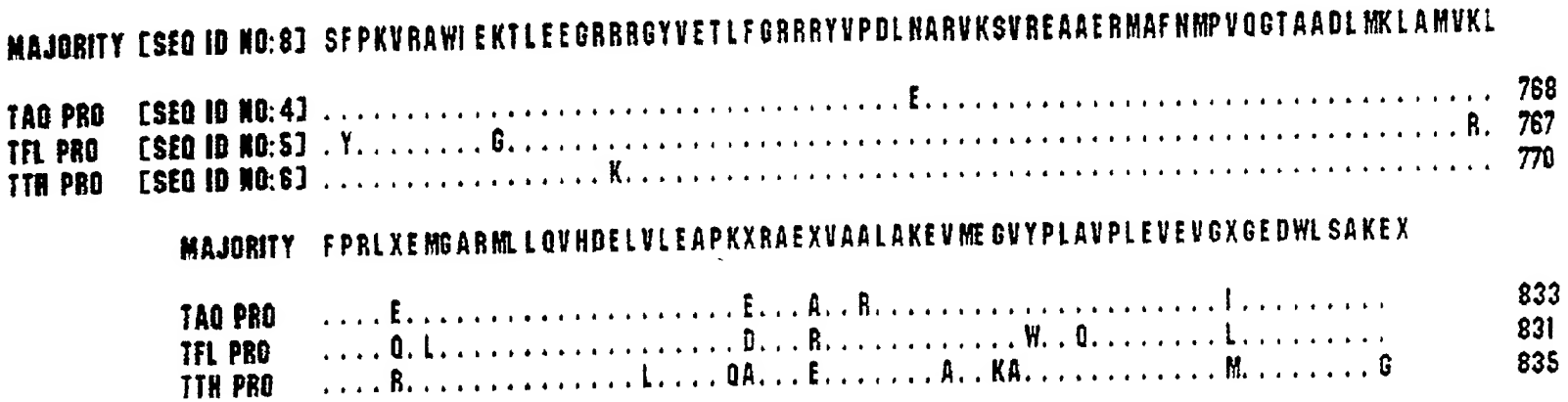

MAJORITY [SEQ ID NO:8] MXAMLPLFEPKGRVLLVDGHHLAYRTFFALKGLTTSRGEPVQAVYGFAKSLLKALKEDG·DAVXVVFDAK
TAQ PRO [SEQ ID NO:4] .RG.....H.....I..... 69
TFL PRO [SEQ ID NO:5] .·.....V.V..... 68
TTH PRO [SEQ ID NO:6] .E.....YK..F..... 70
MAJORITY APSFRHEAYEAYKAGRAPTPEDFPRQLALIKELVDLLGLXRLEVPGYEADDVLATLAKKAEKEGYEVRIL
TAQ PRO .....GG.....A.....S..... 139
TFL PRO .....V.....F.....R..... 138
TTH PRO .....FT..... 140
MAJORITY TADRDLYQLLSDRIAVLHPEGYLITPAWLWEKYGLRPEQWVDYRALXGDPSDNLPGVKGIGEKTAXKLLX
TAQ PRO ...K.....H.....D..A.....T..E.....R...E 209
TFL PRO .....E...I.....Y.....A.....I.....QR.IR 208
TTH PRO .....V...V.....H....E.....F...V.....L...K 210
MAJORITY EWGSLENLLKNLDRVKP·XXREKIXAHMEDLXLSXXLSXVRTDLPLEVDFAXRREPDREGLRAFLERLEF
TAQ PRO .....A.....L..·AI....L...D..K..WD.AK.....K.....R..... 278
TFL PRO .....FQH..Q...·SL...LQ.G..A.A..RK..Q.H.....GR..T.NL..... 277
TTH PRO .....ENV....K..L...R..LE..R.....L.QG..... 280
MAJORITY GSLLHEFGLLEXPKALEEAPWPPPEGAFVGFVLSRPEPMWAELLALAAARXGRVHRAXDPLXGLRDLKEV
TAQ PRO .....S.....K.....D.....G.....PE.YKA.....A 348
TFL PRO .....G...A.....L..SF.....G.WE..L...Q...R.....G. 347
TTH PRO .....A.AP.....K....C.D.....A...A..K..... 350

FIG. 3B

```
MAJORITY [SEQ ID NO:8] RGLLAKDLAVLALREGLDLXPGDDPMLLAYLLDPSNTTPEGVARRYGGEWTEDAGERALLSERLFXNLXX

TAQ PRO  [SEQ ID NO:4] ........S........G.P................................E.....A......A..WG  418
TFL PRO  [SEQ ID NO:5] ..I................F.E......................................A....QT.KE  417
TTH PRO  [SEQ ID NO:6] ............S......V..................................AH........HR..LK  420

               MAJORITY RLEGEERLLWLYXEVEKPLSRVLAHMEATGVRLDVAYLQALSLEVAEEIRRLEEEVFRLAGHPFNLNSRD

               TAQ PRO  ............R...R...A.................R..........A...A................  488
               TFL PRO  ..K.........E...........R....................EA.V.Q...................  487
               TTH PRO  ......K.....H...............................L.........................  490

               MAJORITY QLERVLFDELGLPAIGKTEKTGKRSTSAAVLEALREAHPIVEKILQYRELTKLKNTYIDPLPXLVHPRTG

               TAQ PRO  ......................................................S.......D.I.....  558
               TFL PRO  ........................................DR....................A....K..  557
               TTH PRO  ..........R...L...Q...........................H..........V....S.......  560

               MAJORITY RLHTRFNQTATATGRLSSSDPNLQNIPVRTPLGQRIRRAFVAEEGWXLVALDYSQIELRVLAHLSGDENL

               TAQ PRO  ........................................I.....L.......................  628
               TFL PRO  ..............................................V..V....................  627
               TTH PRO  ...........................................A..A.......................  630

               MAJORITY IRVFQEGRDIHTQTASWMFGVPPEAVDPLMRRAAKTINFGVLYGMSAHRLSQELAIPYEEAVAFIERYFQ

               TAQ PRO  ............E.........R......................................Q........  698
               TFL PRO  .....................S..G..........................G..S...............  697
               TTH PRO  .......K............................V.................................  700
```

FIG. 3C


MAJORITY [SEQ ID NO:8] SFPKVRAWIEKTLEEGRRRGYVETLFGRRRYVPDLNARVKSVREAAERMAFNMPVQGTAADLMKLAMVKL
TAQ PRO [SEQ ID NO:4] 768
TFL PRO [SEQ ID NO:5] 767
TTH PRO [SEQ ID NO:6] 770
MAJORITY FPRLXEMGARMLLQVHDELVLEAPKXRAEXVAALAKEVMEGVYPLAVPLEVEVGXGEDWLSAKEX
TAQ PRO 833
TFL PRO 831
TTH PRO 835

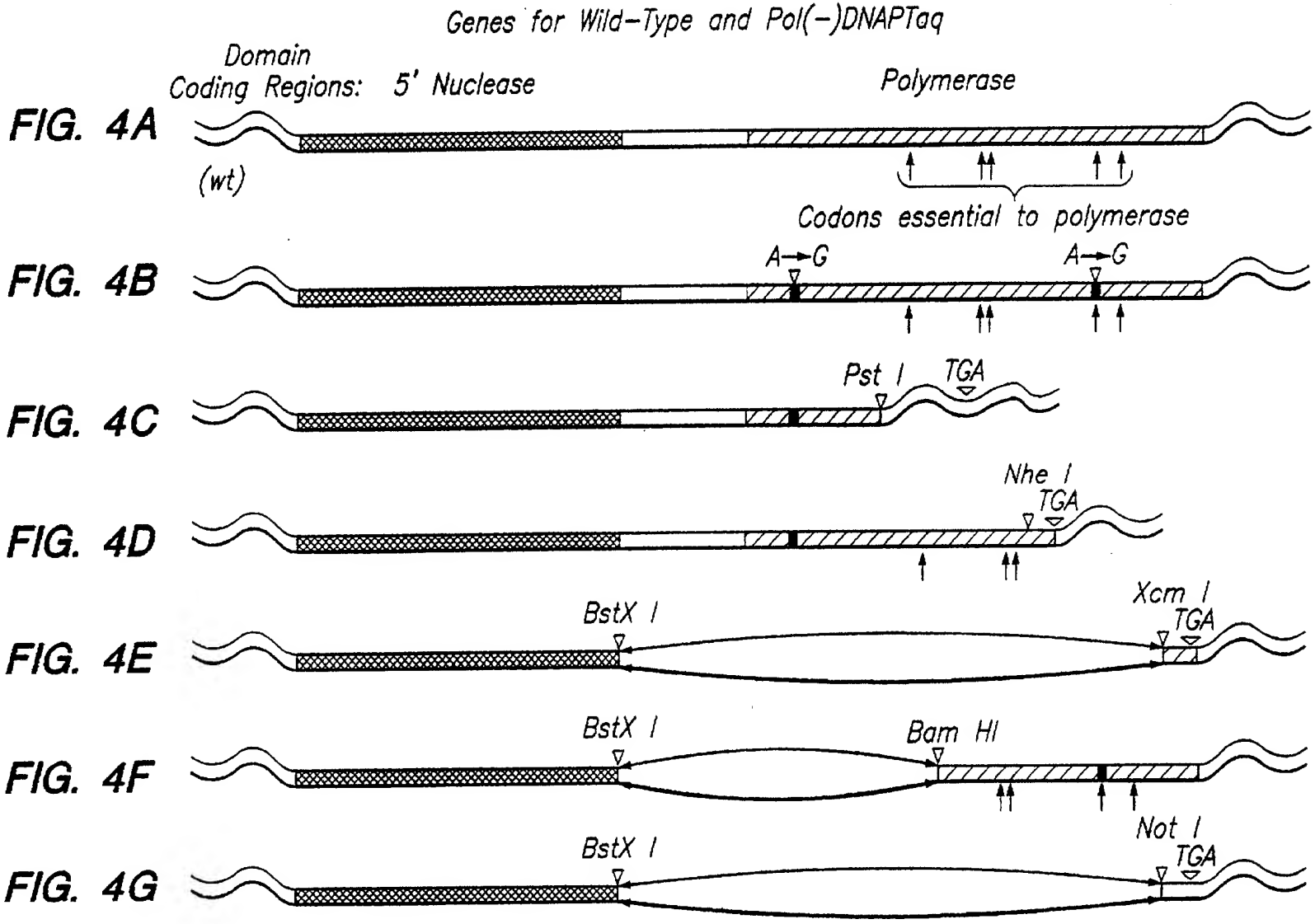


FIG. 4A

FIG. 4B

FIG. 4C

FIG. 4D

FIG. 4E

FIG. 4F

FIG. 4G

Genes for Wild-Type and Pol(-) DNAPTfl

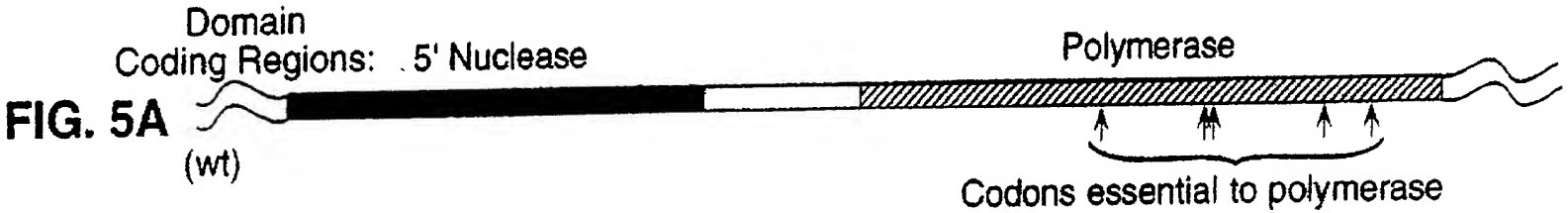


FIG. 5A

FIG. 5B

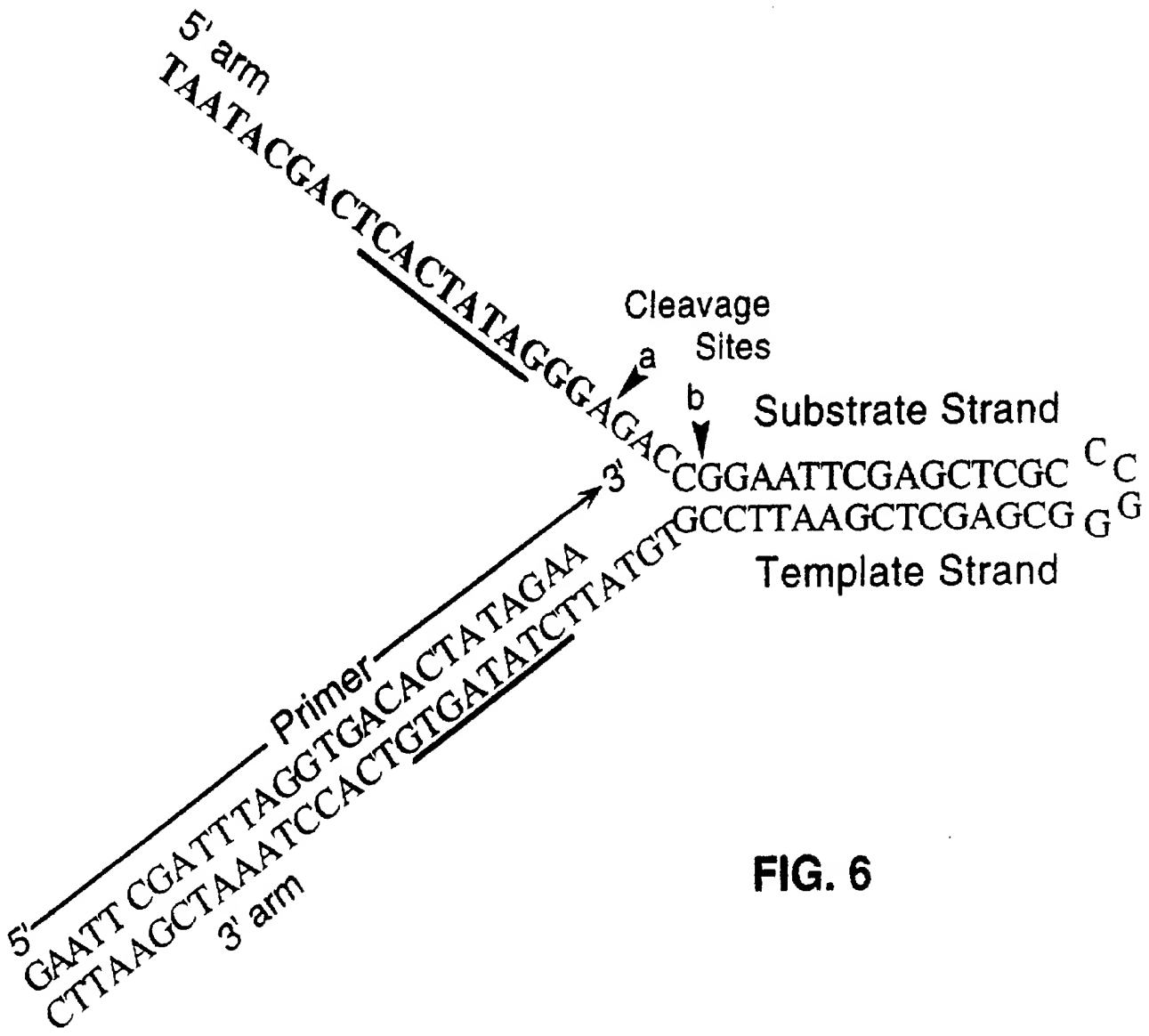

5' arm
TAATACGACTCACTATAGGGAGACC
Cleavage
Sites
a
b
Substrate Strand
3'
CGGAATTCGAGCTCGC C C
GCCTTAAGCTCGAGCG G G
Template Strand
Primer
5'
GAATT CGATTTAGGTGACACTATAGAA
CTTAAGCTAAATCCACTGTGATATCTTATGT
3' arm

FIG. 6

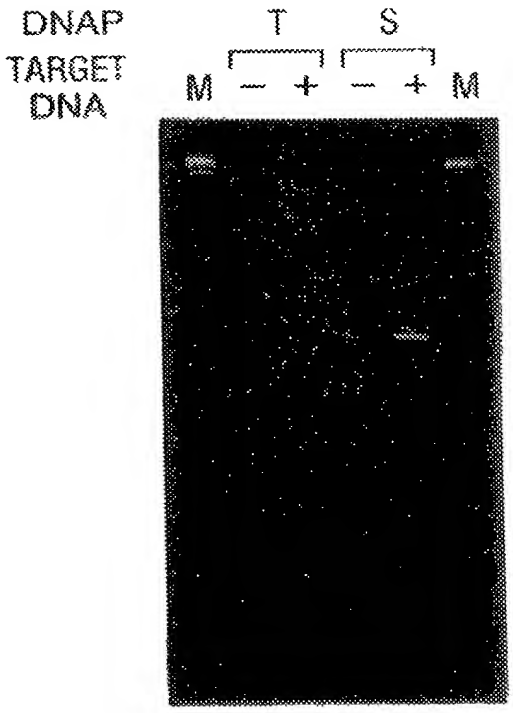


FIG. 7

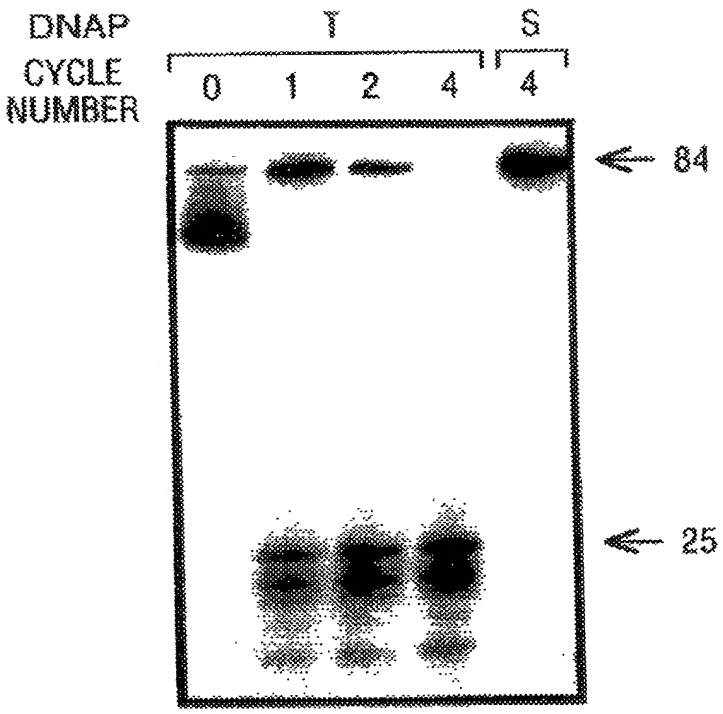


FIG. 8

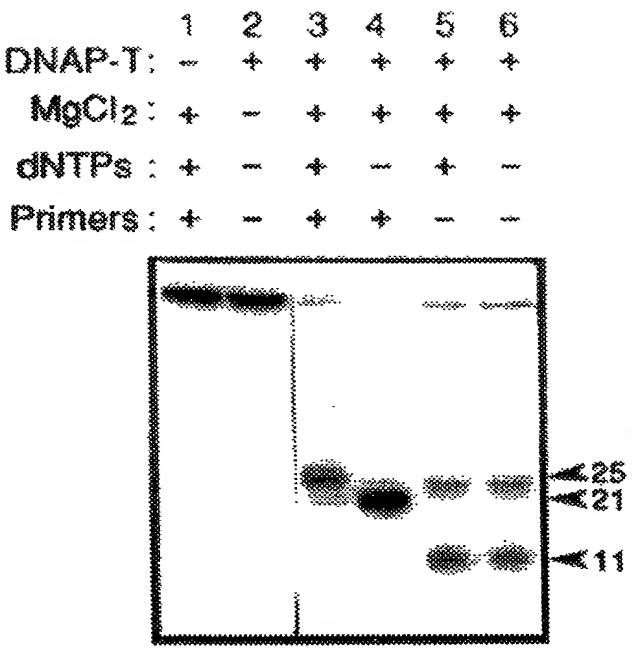


FIG. 9A

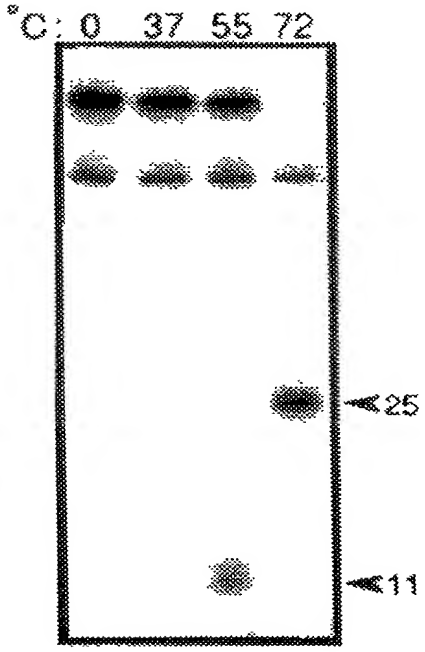


FIG. 9B

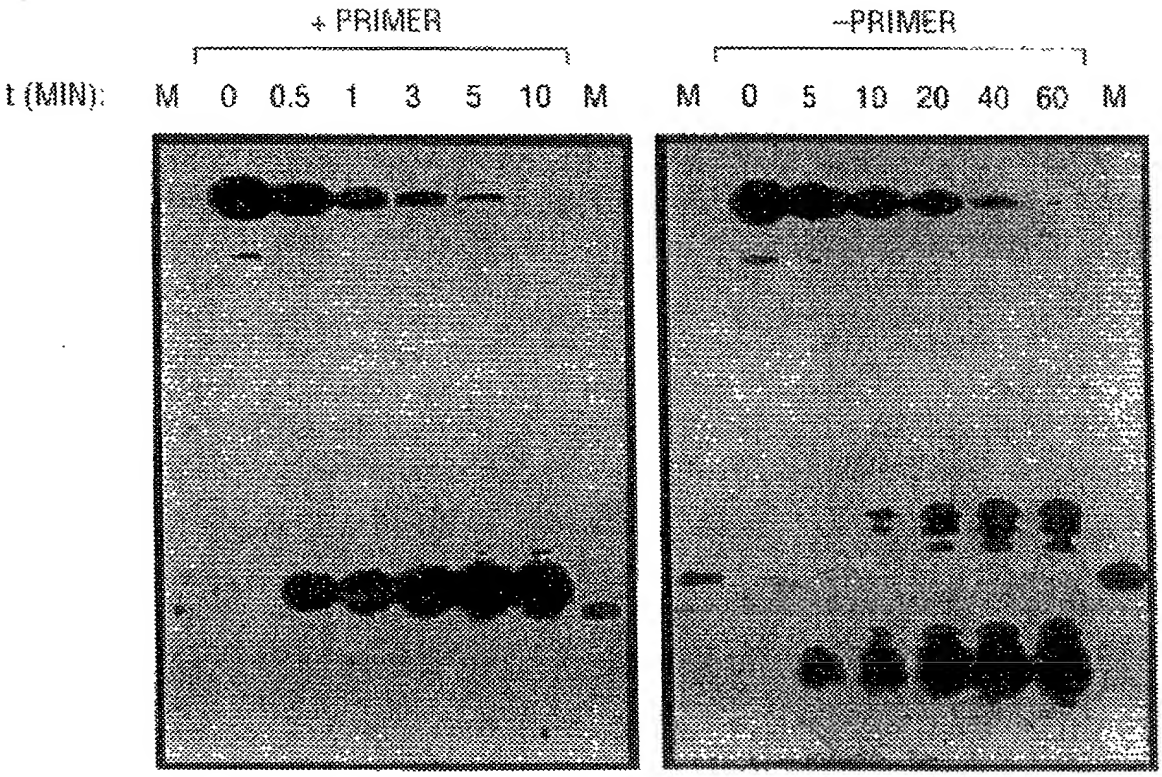


FIG. 10A

FIG. 10B

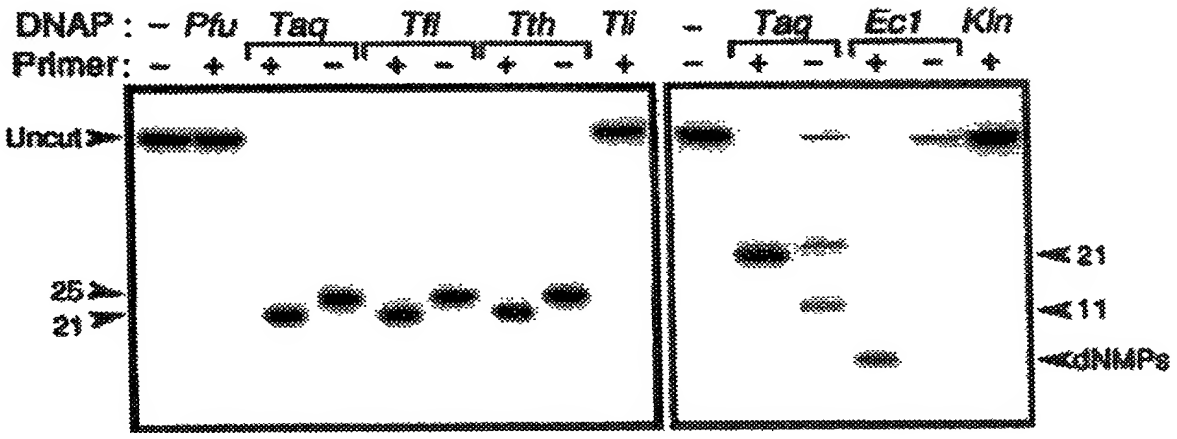
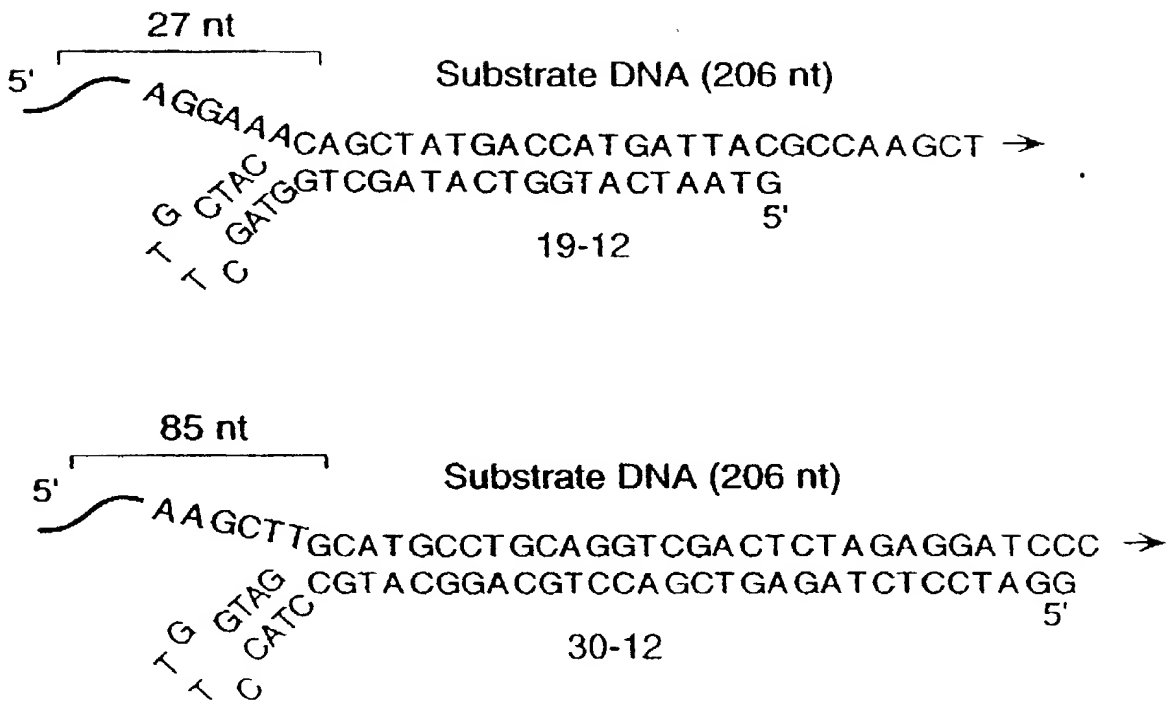


FIG. 11A

FIG. 11B

FIG. 12A


27 nt
5'
Substrate DNA (206 nt)
AGGAAACAGCTATGACCATGATTACGCCAAGCT
TG CTAC
T GATGGTCGATACTGGTACTAATG
T C
5'
19-12
85 nt
5'
Substrate DNA (206 nt)
AAGCTTGCATGCCTGCAGGTCGACTCTAGAGGATCCC
TG GTAG
T CATC CGTACGGACGTCCAGCTGAGATCTCCTAGG
T C
5'
30-12

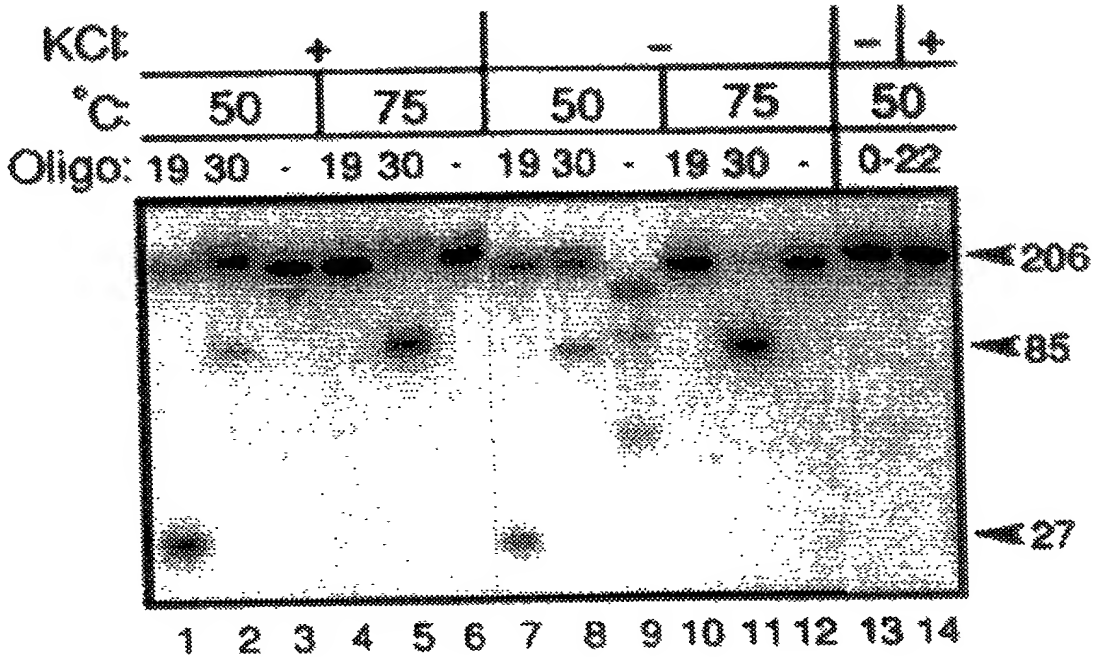


FIG. 12B

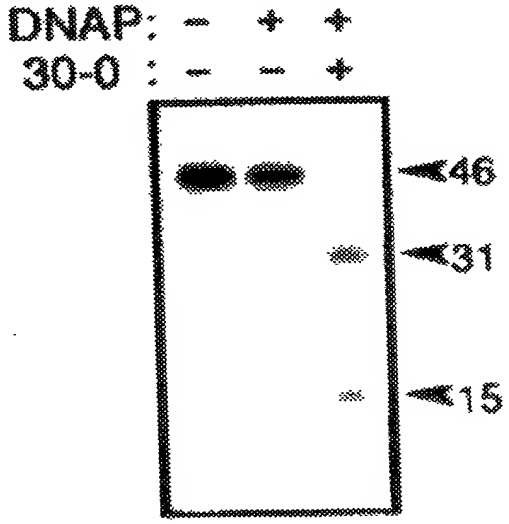


FIG. 13B

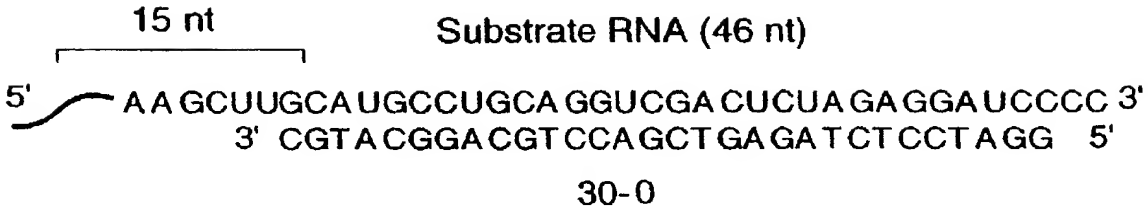


FIG. 13A

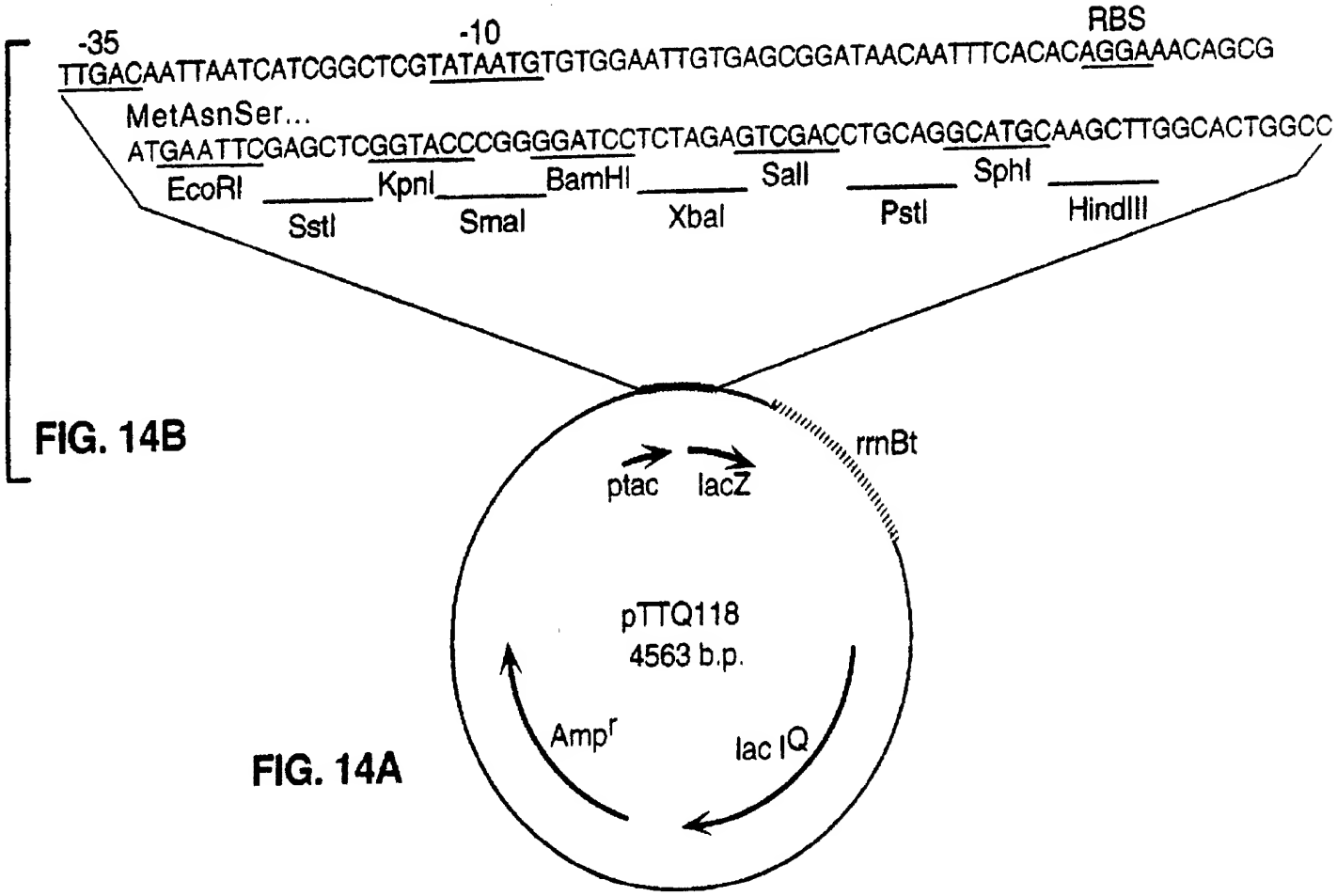


FIG. 14B

FIG. 14A

RBS: Ribosome binding site
ptac: Synthetic tac promoter
lac I^Q: Lac repressor gene

lacZ: Beta-galactosidase alpha fragment
rrnBt: E. coli rrnB transcription terminator

FIG. 14C

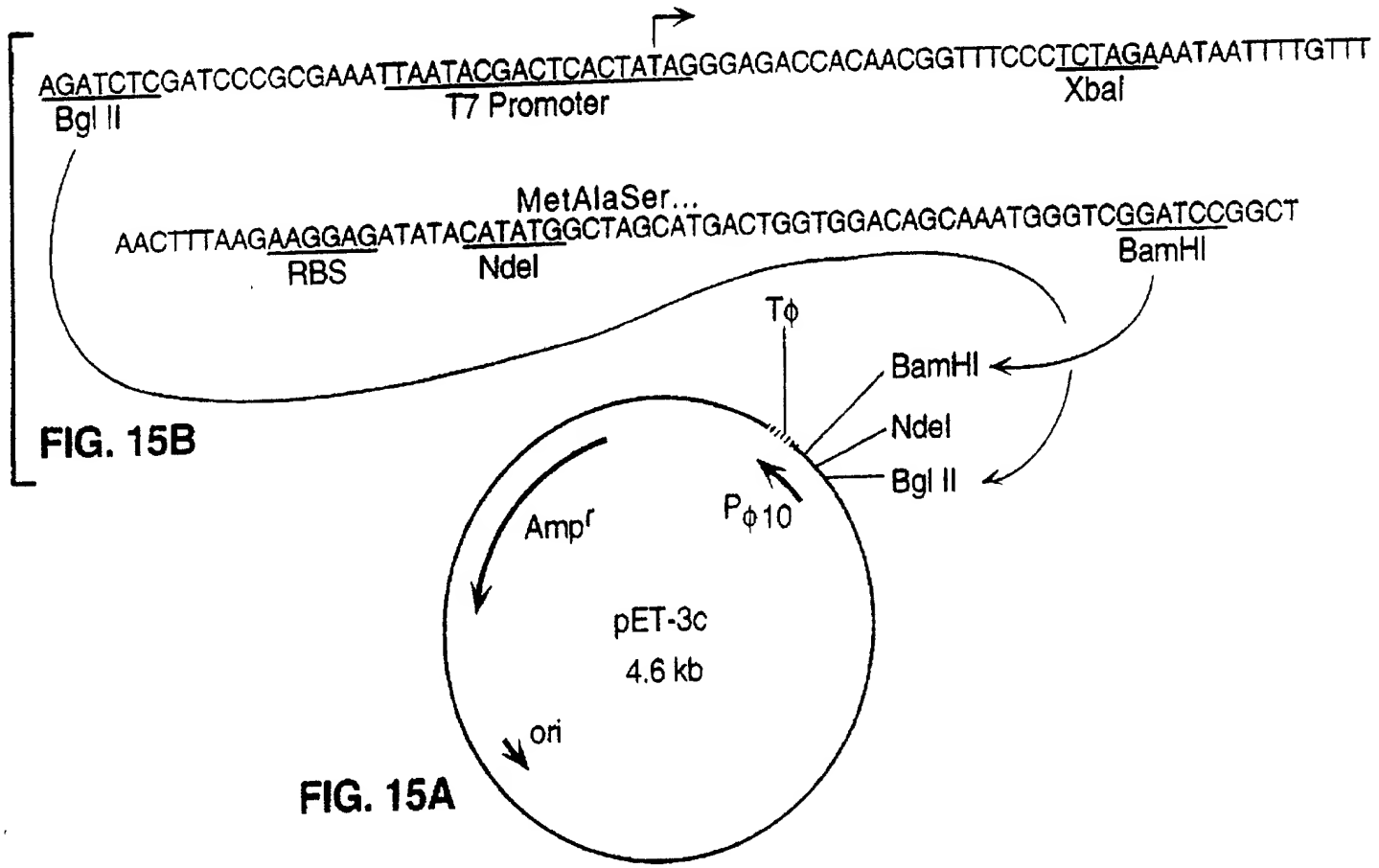


FIG. 15B

FIG. 15A

$P_{\phi 10}$: Bacteriophage T7 ϕ10 promoter

RBS: Ribosome binding site

Tϕ: T7 ϕ Terminator

FIG. 15C

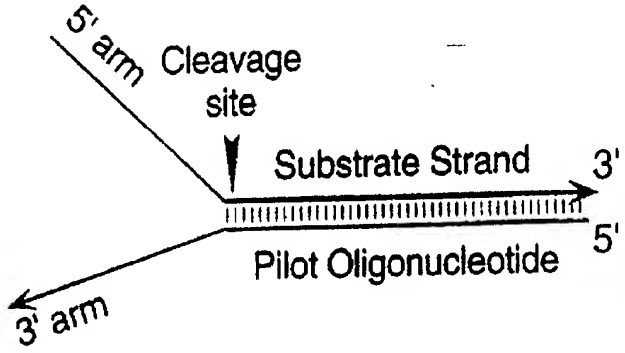


FIG. 16A

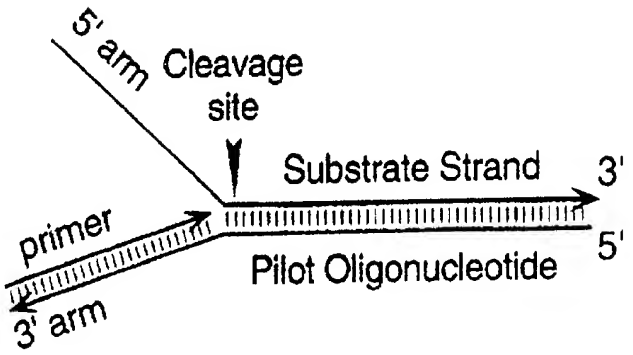


FIG. 16B

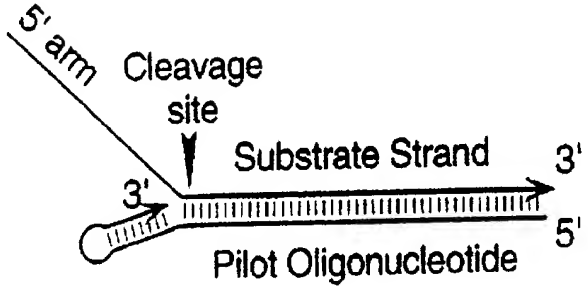


FIG. 16C

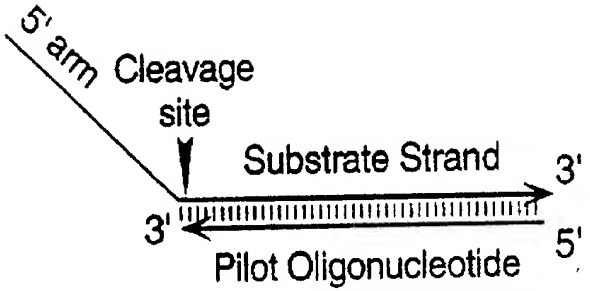


FIG. 16D

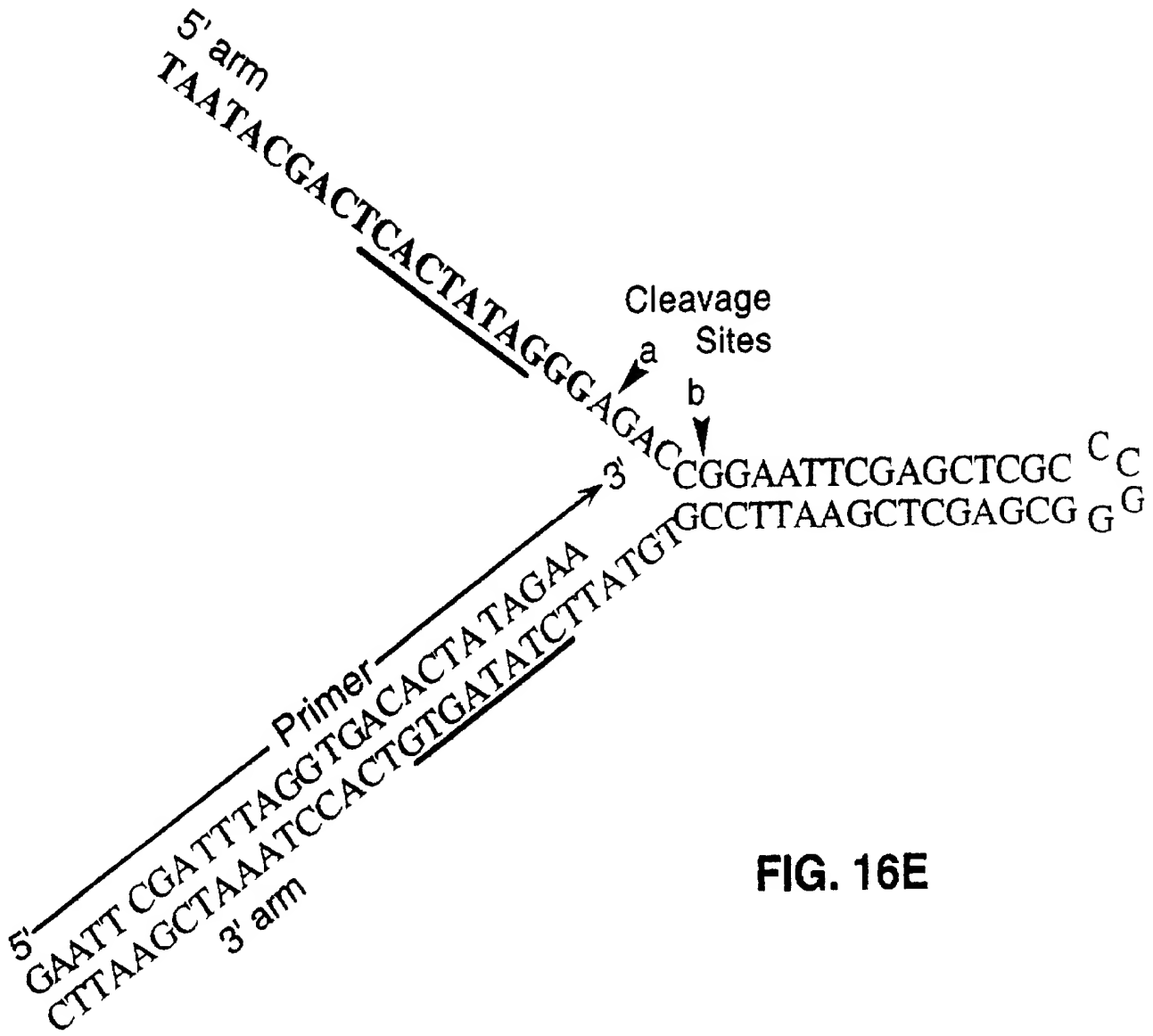

5' arm
TAATACGACTCACTATAGGGAGACC
Cleavage
Sites
a
b
3'
CGGAATTCGAGCTCGC C C
GCCTTAAGCTCGAGCG G G
Primer
5'
GAATT CGATTTAGGTGACACTATAGAA
CTTAAGCTAAATCCACTGTGATATCTTATGT
3' arm

FIG. 16E

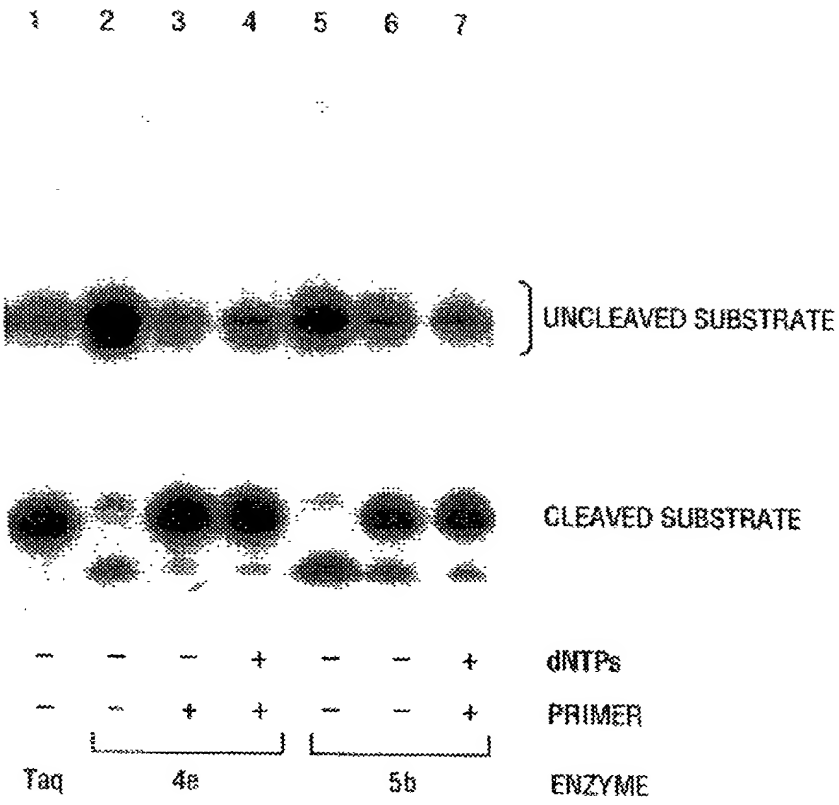

1 2 3 4 5 6 7
UNCLEAVED SUBSTRATE
CLEAVED SUBSTRATE
– – – + – – + dNTPs
– – + + – – + PRIMER
Taq 4a 5b ENZYME

FIG. 17

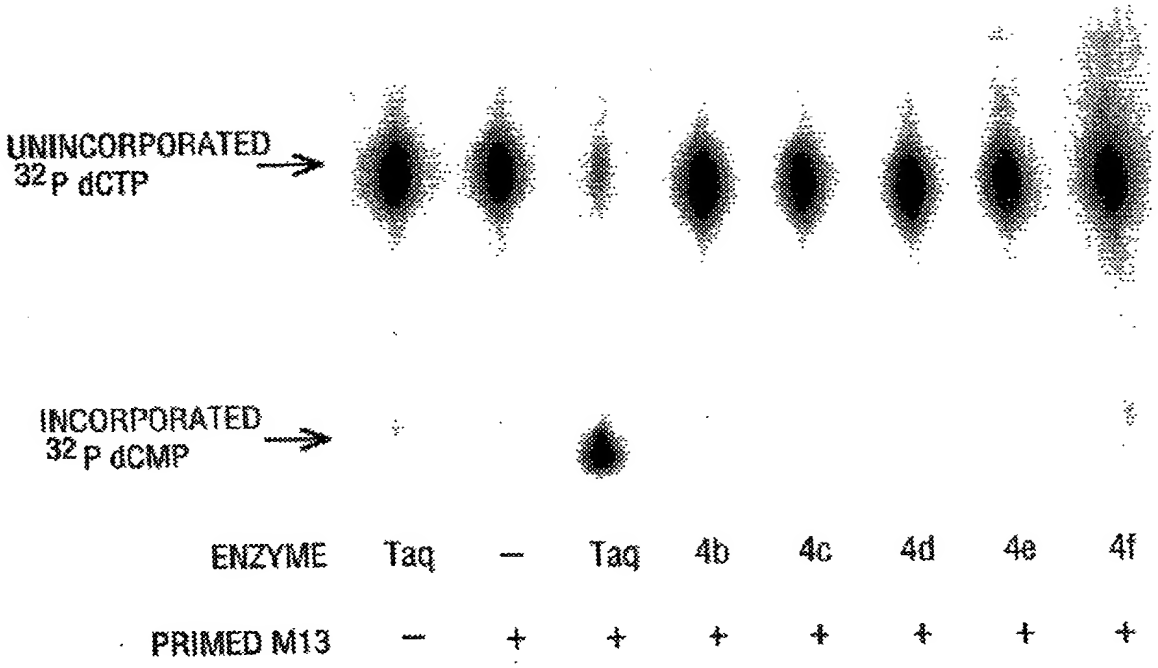

UNINCORPORATED
32 P dCTP
INCORPORATED
32 P dCMP
ENZYME Taq — Taq 4b 4c 4d 4e 4f
PRIMED M13 — + + + + + + +

FIG. 18

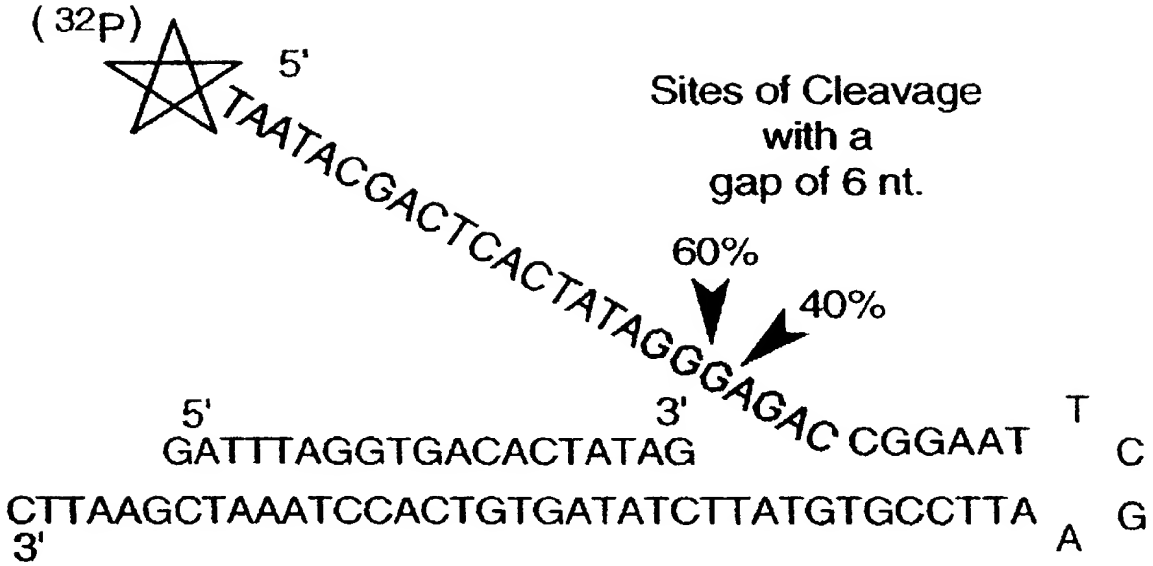

(32P)
5'
TAATACGACTCACTATAGGGAGAC
Sites of Cleavage
with a
gap of 6 nt.
60%
40%
5'
3'
GATTTAGGTGACACTATAG
CGGAAT
T
C
CTTAAGCTAAATCCACTGTGATATCTTATGTGCCTTA
A
G
3'

FIG. 19A

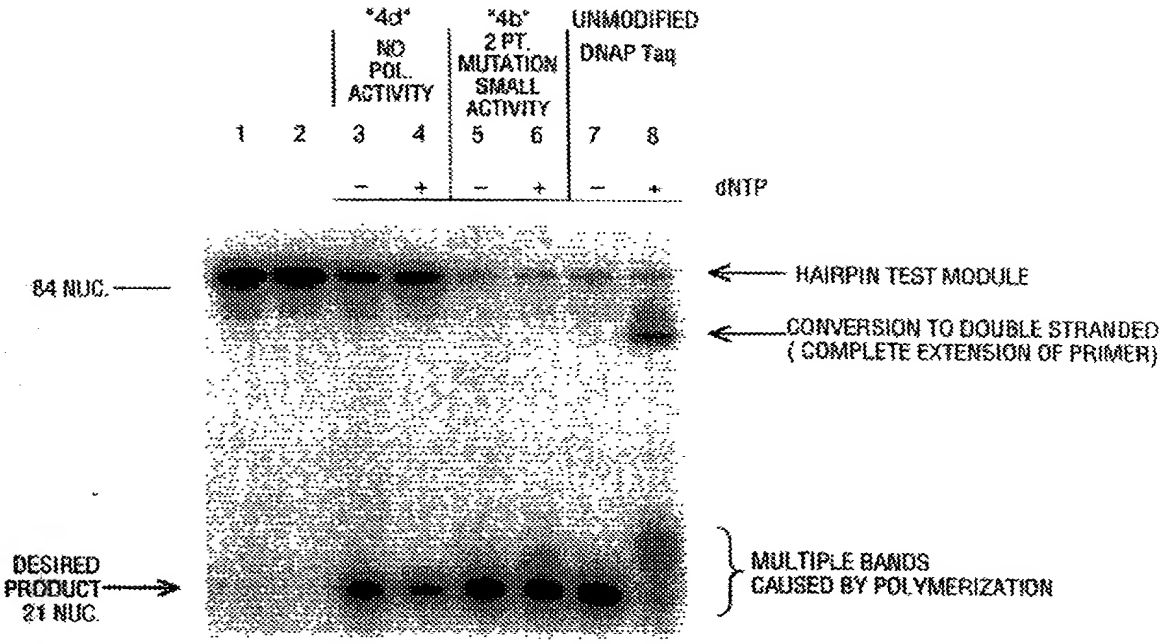

"4d"
NO POL. ACTIVITY
"4b"
2 PT. MUTATION SMALL ACTIVITY
UNMODIFIED
DNAP Taq
1 2 3 4 5 6 7 8
- + - + - +
dNTP
84 NUC.
HAIRPIN TEST MODULE
CONVERSION TO DOUBLE STRANDED
(COMPLETE EXTENSION OF PRIMER)
DESIRED PRODUCT
21 NUC.
MULTIPLE BANDS
CAUSED BY POLYMERIZATION
SOME ABERRANT CLEAVAGE WITH "4b"
BECAUSE OF RESIDUAL POLYMERASE ACTIVITY.

FIG. 19B

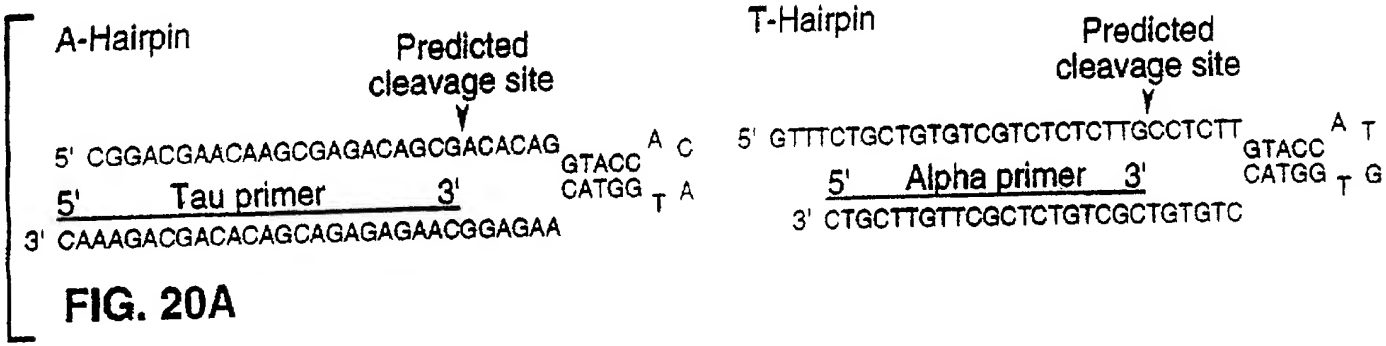


FIG. 20A

Sequence of alpha primer:
5' GACGAACAAGCGAGACAGCG 3'

FIG. 20B

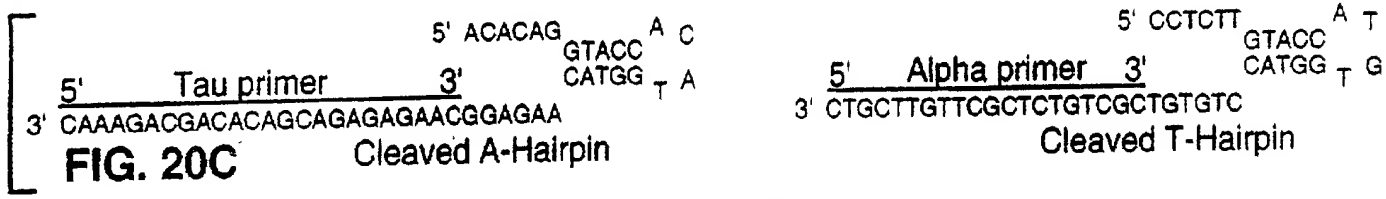


FIG. 20C

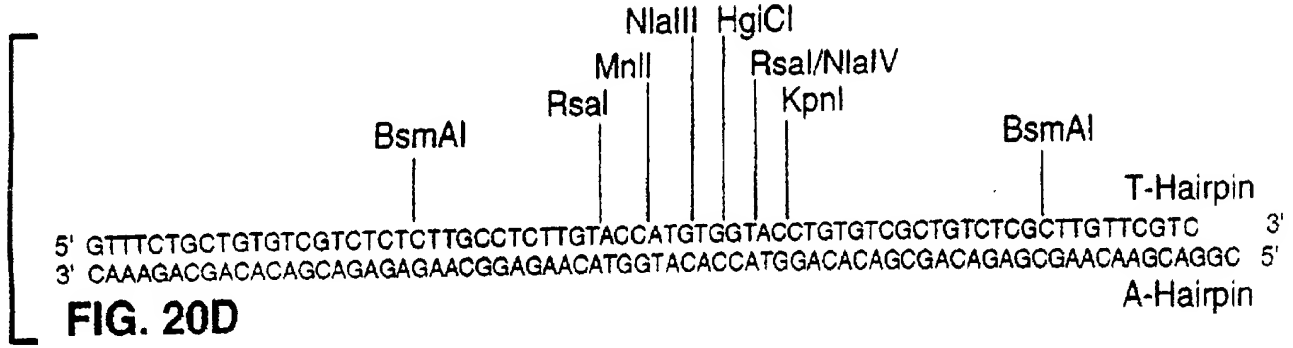


FIG. 20D

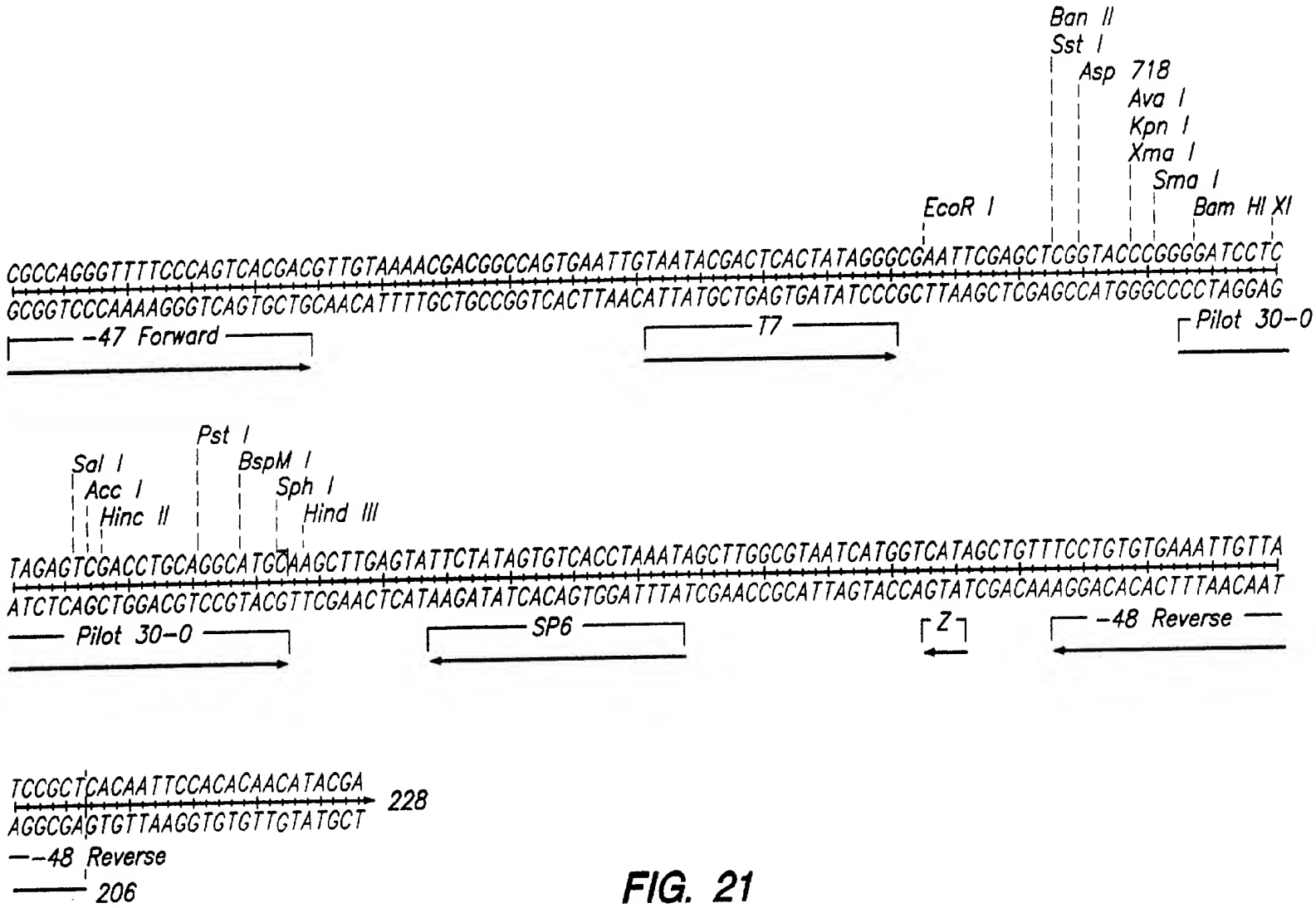

Ban II
Sst I
Asp 718
Ava I
Kpn I
Xma I
Sma I
EcoR I
Bam HI XI
CGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTCGAGCTCGGTACCCGGGGATCCTC
GCGGTCCCAAAAGGGTCAGTGCTGCAACATTTTGCTGCCGGTCACTTAACATTATGCTGAGTGATATCCCGCTTAAGCTCGAGCCATGGGCCCCTAGGAG
-47 Forward
T7
Pilot 30-0
Pst I
Sal I
BspM I
Acc I
Sph I
Hinc II
Hind III
TAGAGTCGACCTGCAGGCATGCAAGCTTGAGTATTCTATAGTGTCACCTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTA
ATCTCAGCTGGACGTCCGTACGTTCGAACTCATAAGATATCACAGTGGATTTATCGAACCGCATTAGTACCAGTATCGACAAAGGACACACTTTAACAAT
Pilot 30-0
SP6
Z
-48 Reverse
TCCGCTCACAATTCCACACAACATACGA
AGGCGAGTGTTAAGGTGTGTTGTATGCT
228
--48 Reverse
206

FIG. 21

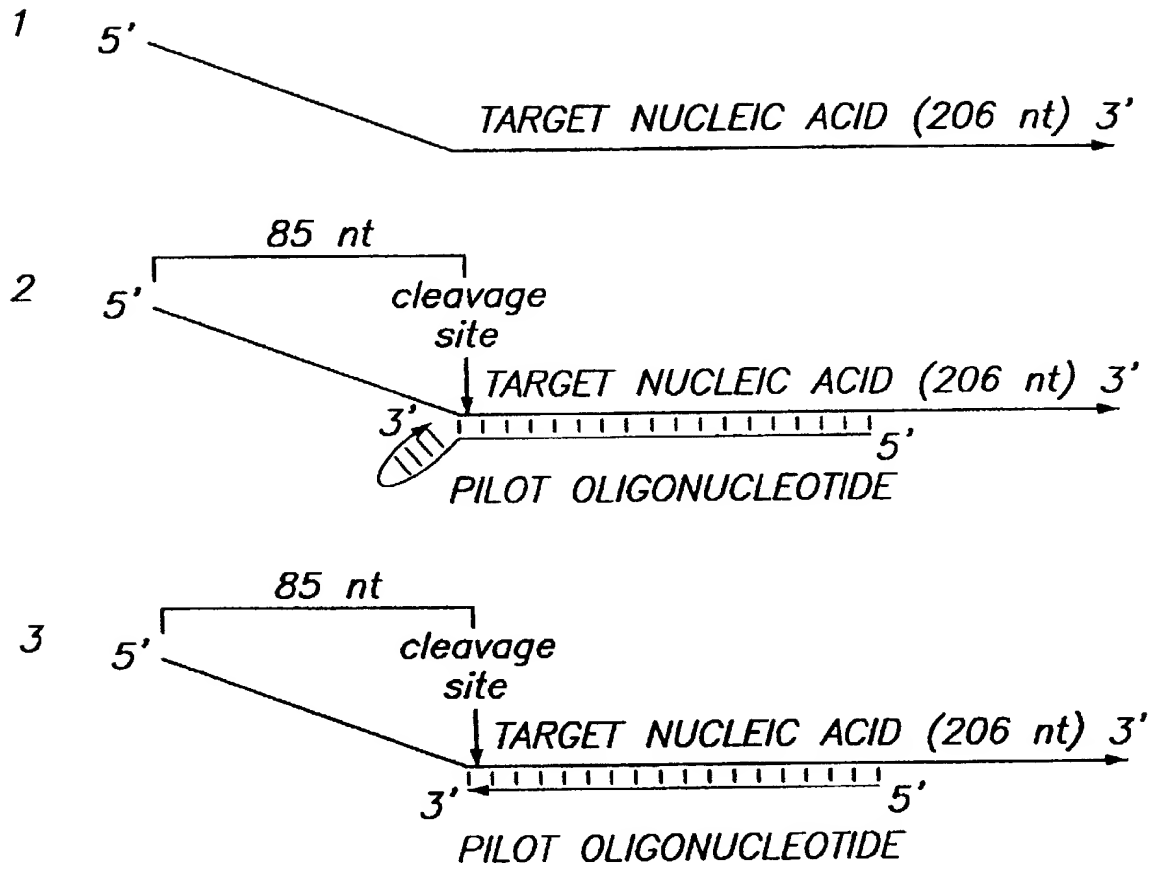


FIG. 22A

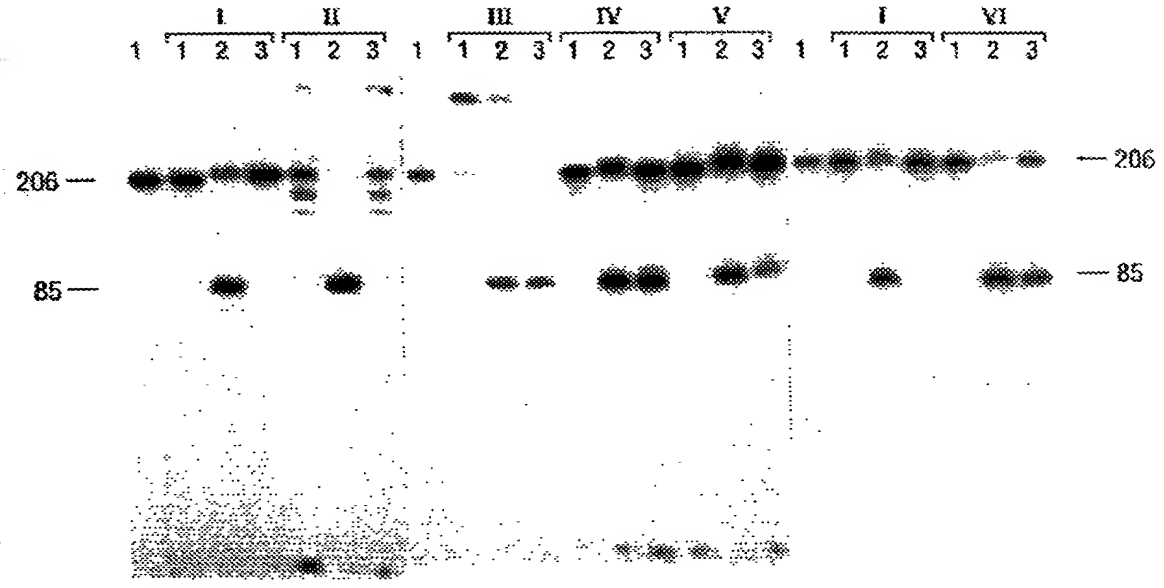


FIG. 22B

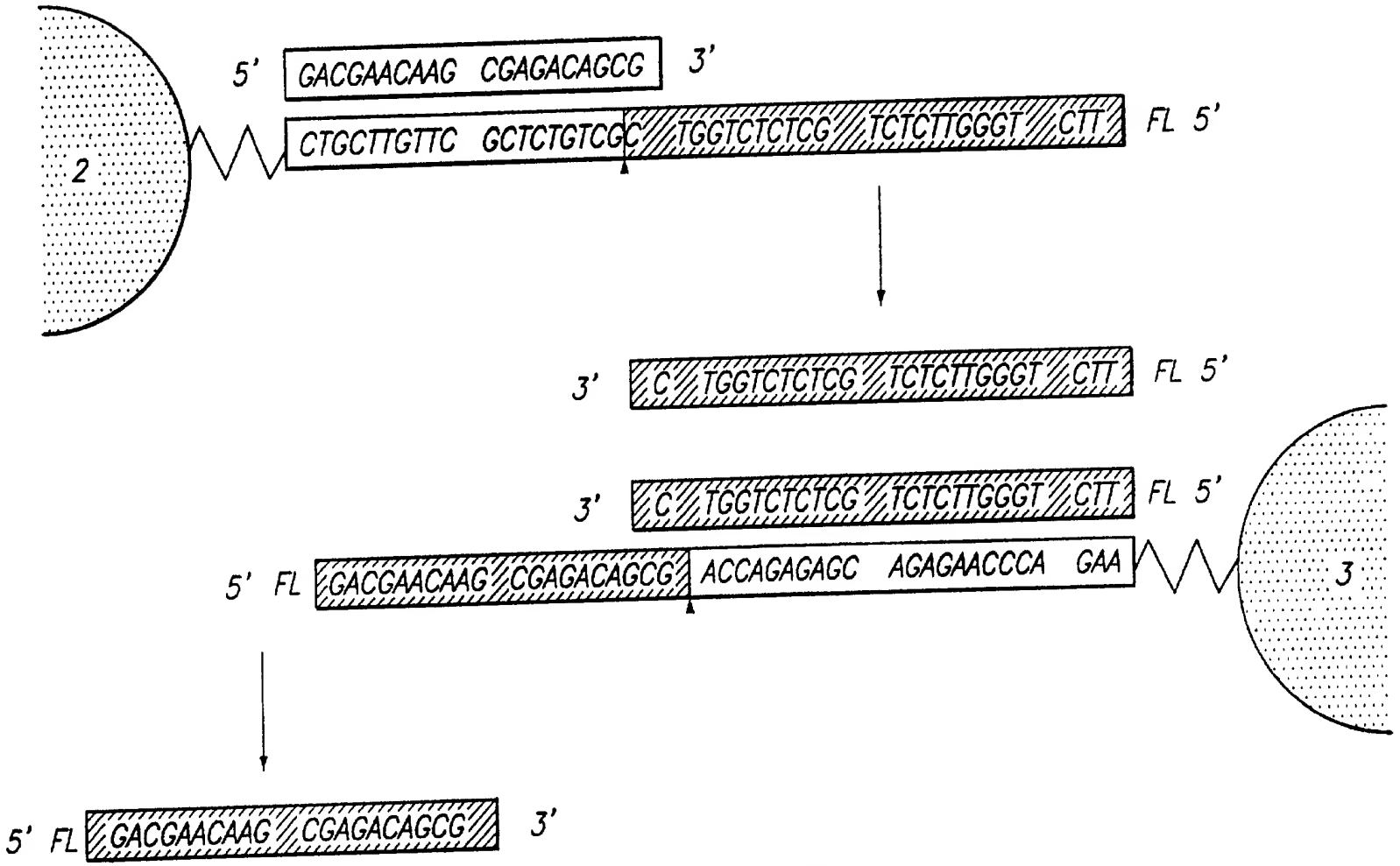

5'
GACGAACAAG CGAGACAGCG
3'
2
CTGCTTGTTC GCTCTGTCGC
TGGTCTCTCG TCTCTTGGGT CTT
FL 5'
3'
C TGGTCTCTCG TCTCTTGGGT CTT
FL 5'
3'
C TGGTCTCTCG TCTCTTGGGT CTT
FL 5'
5' FL
GACGAACAAG CGAGACAGCG
ACCAGAGAGC AGAGAACCCA GAA
3
5' FL
GACGAACAAG CGAGACAGCG
3'

FIG. 23

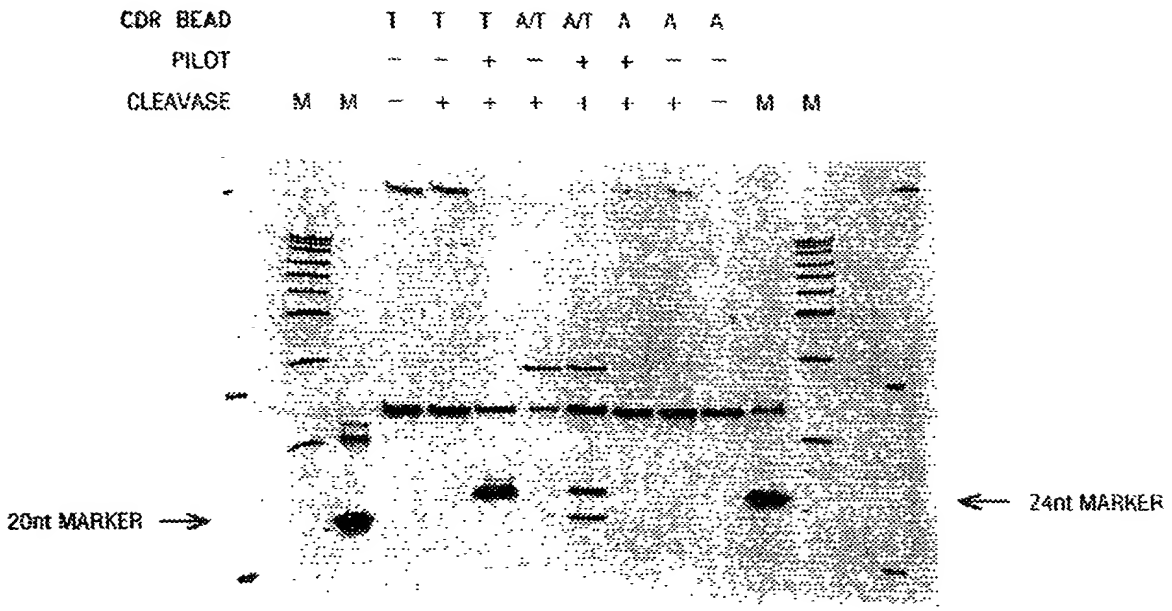

CDR BEAD
PILOT
CLEAVASE
T T T A/T A/T A A A
M M – + + + + + + – M M
20nt MARKER
24nt MARKER

FIG. 24

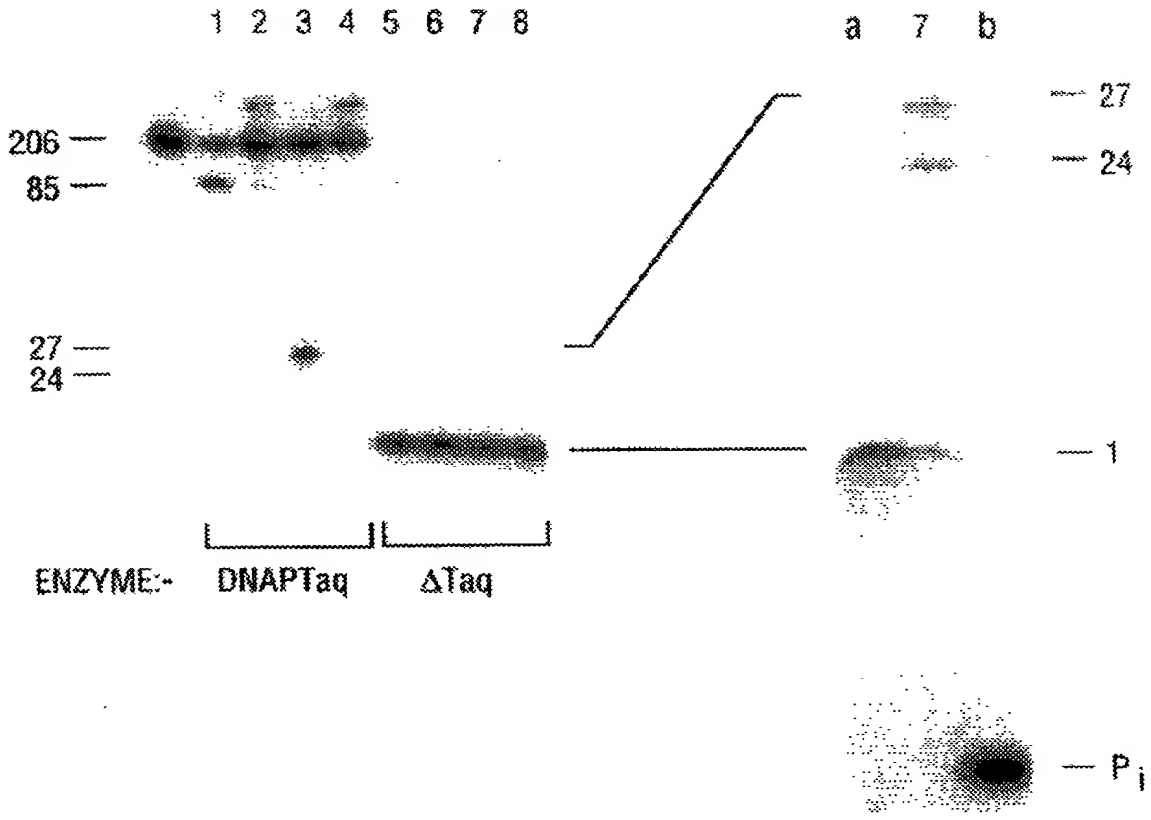


FIG. 25A

FIG. 25B

FIG. 26A

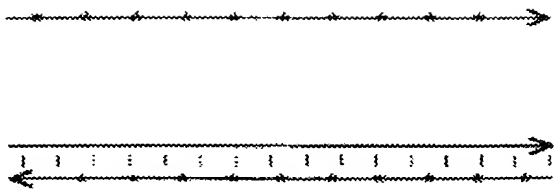
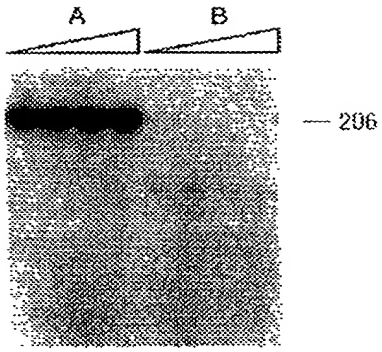


FIG. 26B



^{32}P

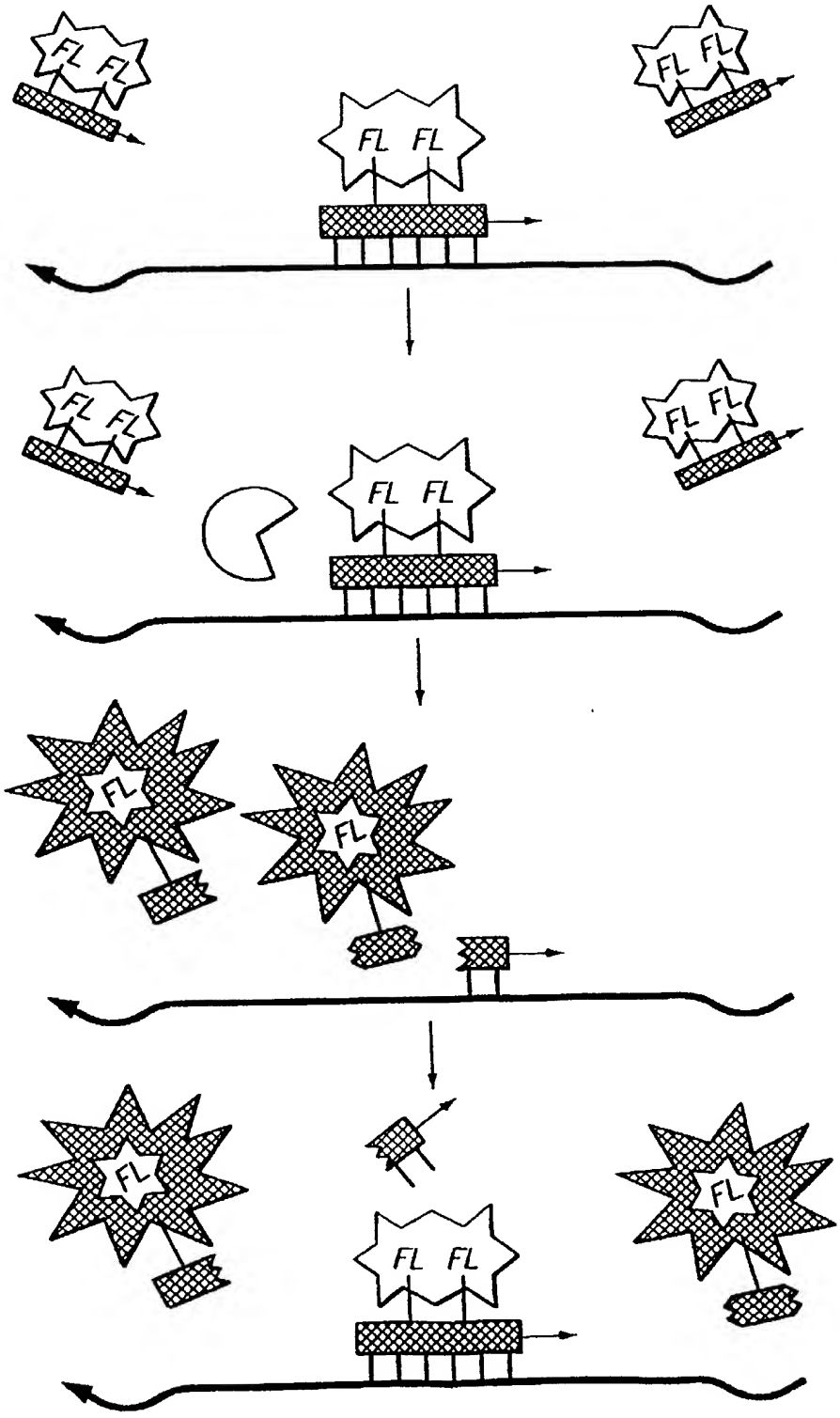


FIG. 27

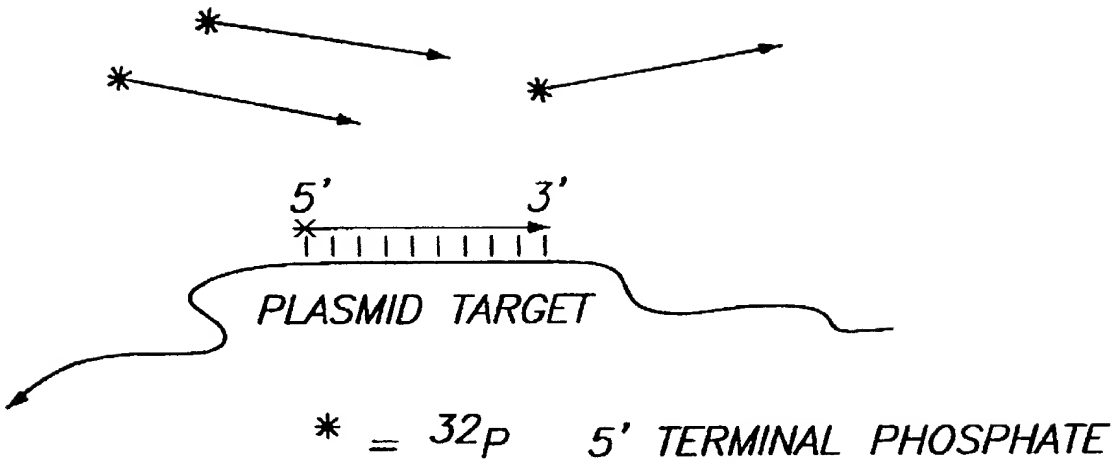


FIG. 28A

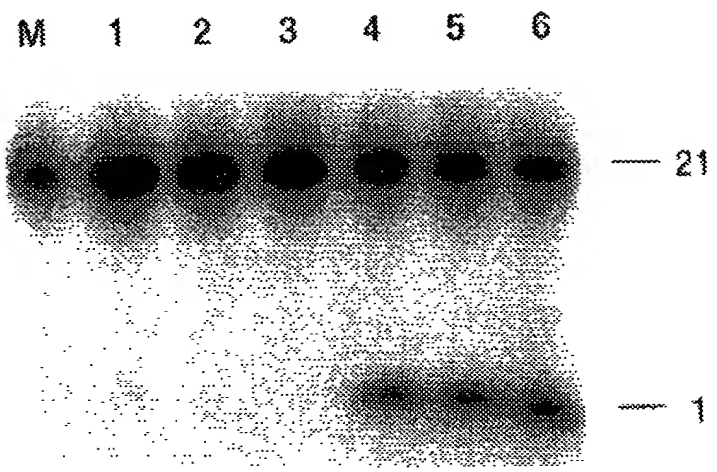


FIG. 28B

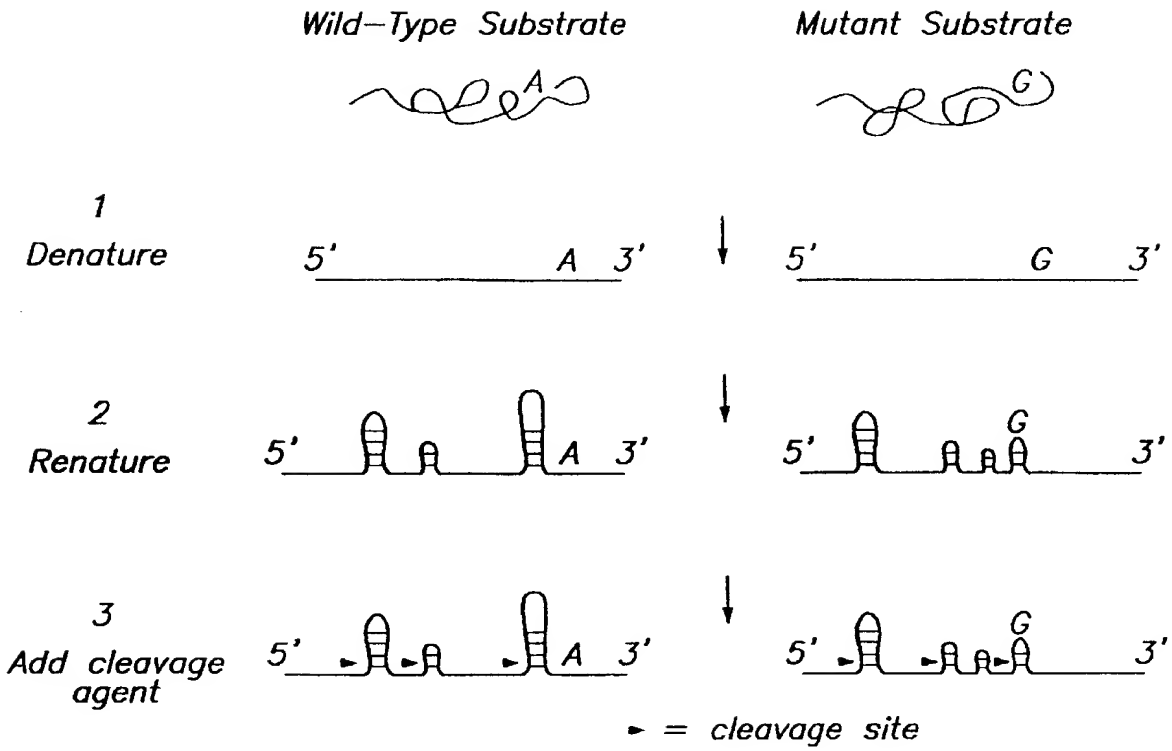


FIG. 29

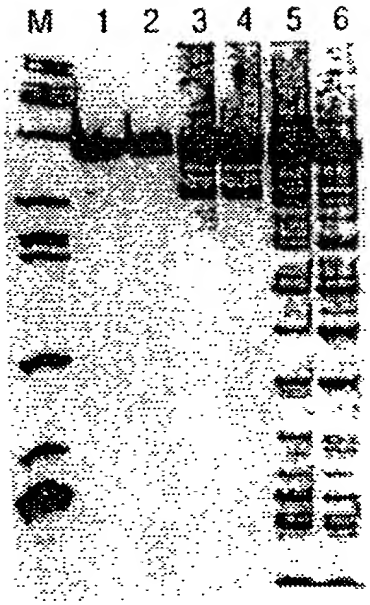


FIG. 30

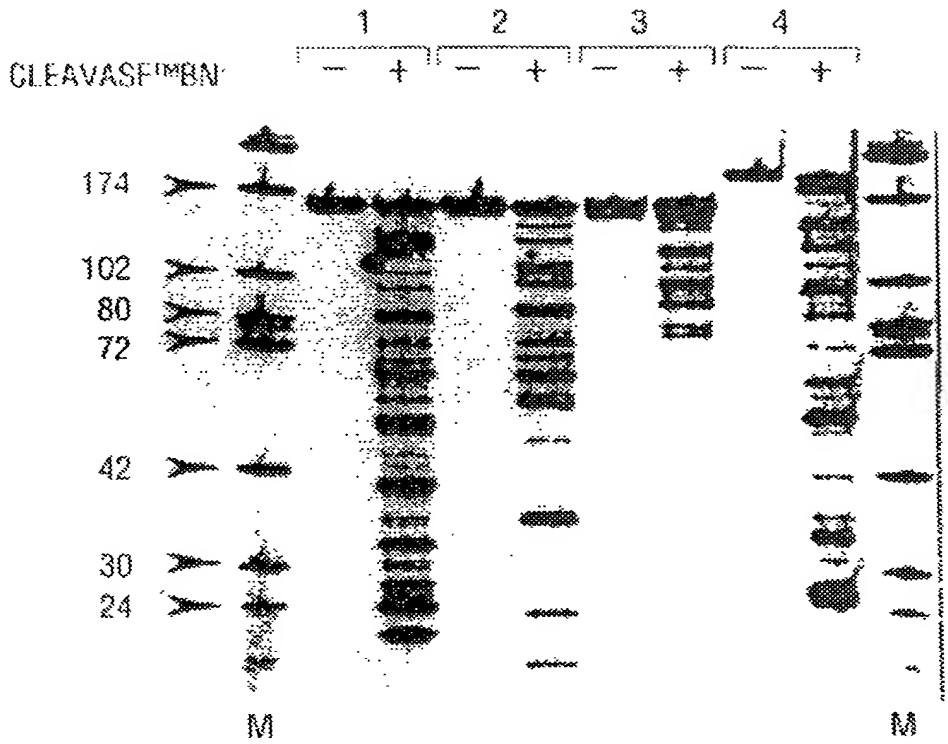


FIG. 31

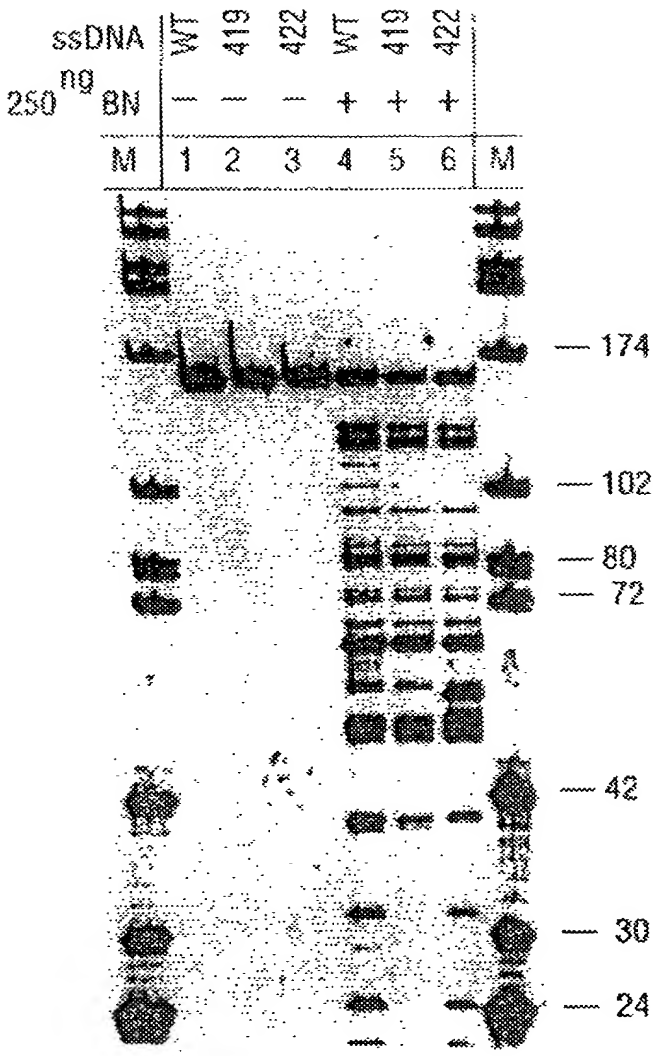

ssDNA
WT
419
422
WT
419
422
250 ng BN
—
—
—
+
+
+
M
1
2
3
4
5
6
M
174
102
80
72
42
30
24

FIG. 32

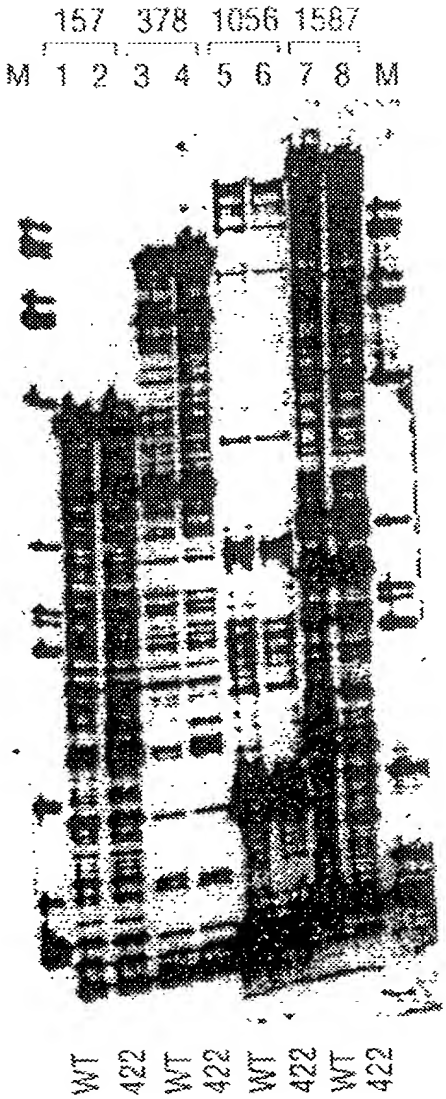


FIG. 33

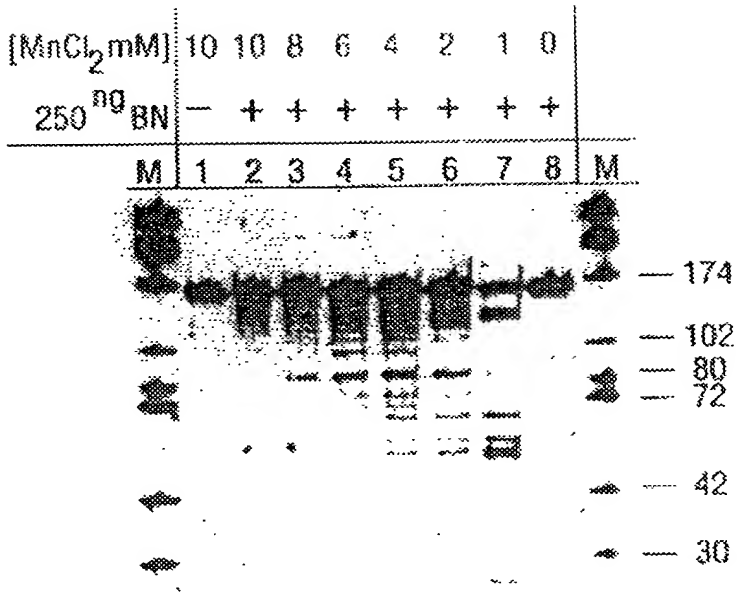


FIG. 34

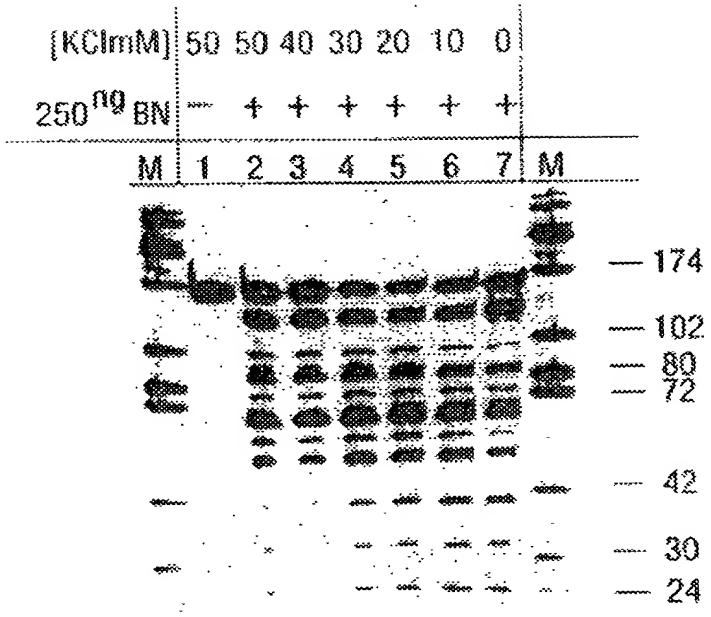

[KCl mM] 50 50 40 30 20 10 0
250 ng BN — + + + + + +
M 1 2 3 4 5 6 7 M
174
102
80
72
42
30
24

FIG. 35

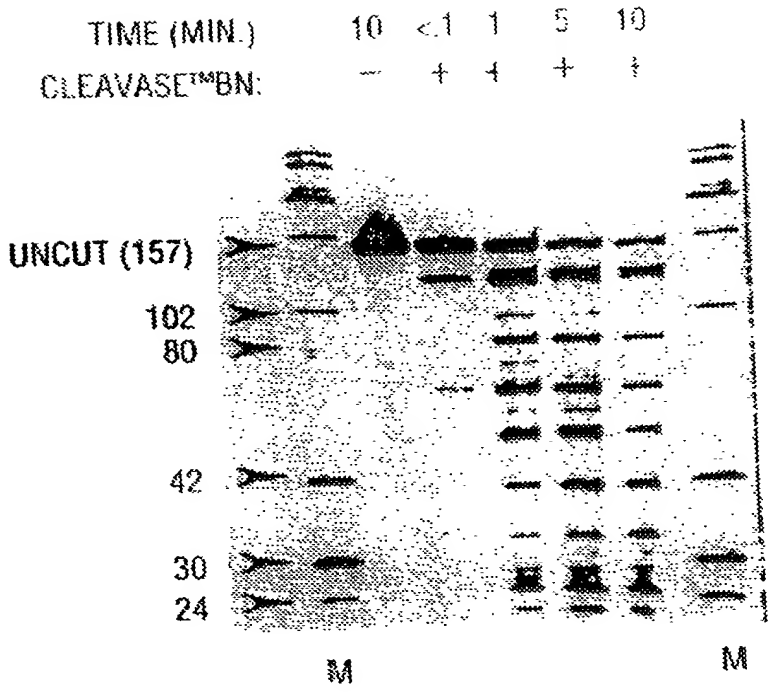


FIG. 36

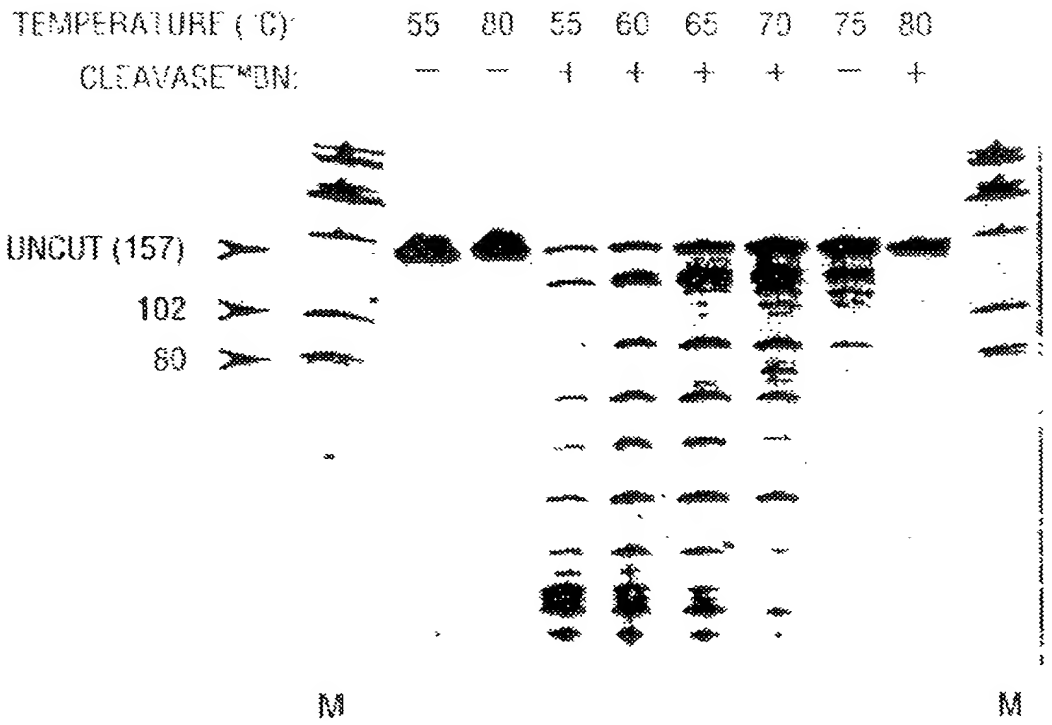

TEMPERATURE (°C)
55 80 55 60 65 70 75 80
CLEAVASE™ON:
— — + + + + — +
UNCUT (157)
102
80
M
M

FIG. 37

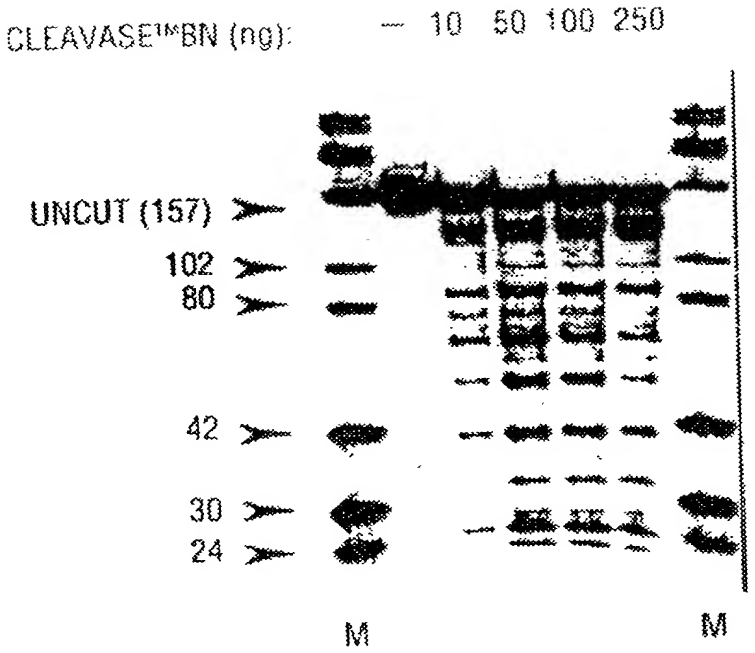


FIG. 38

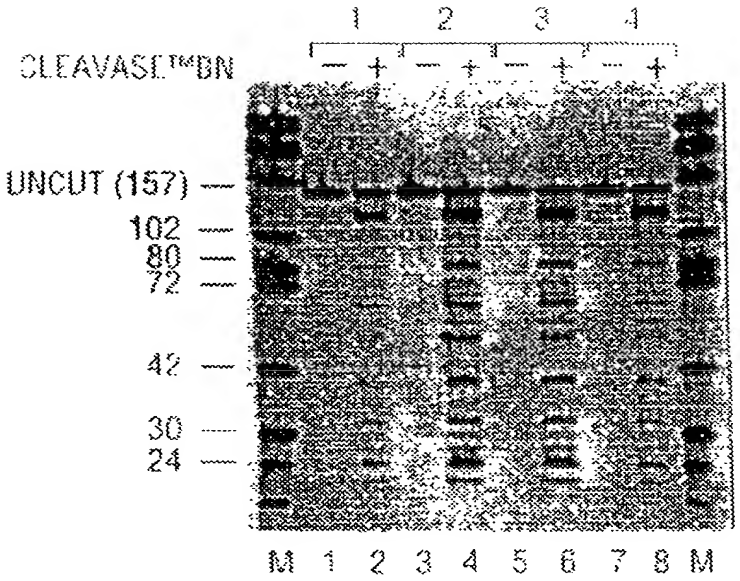


FIG. 39

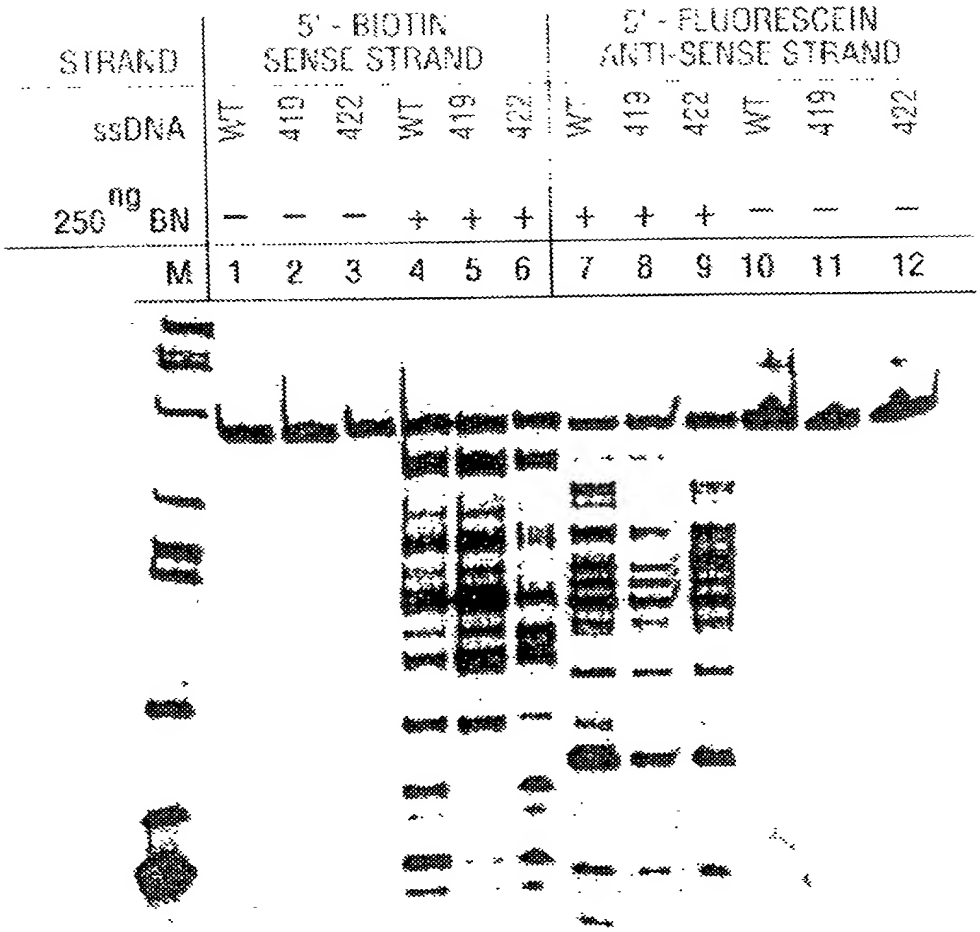


FIG. 40

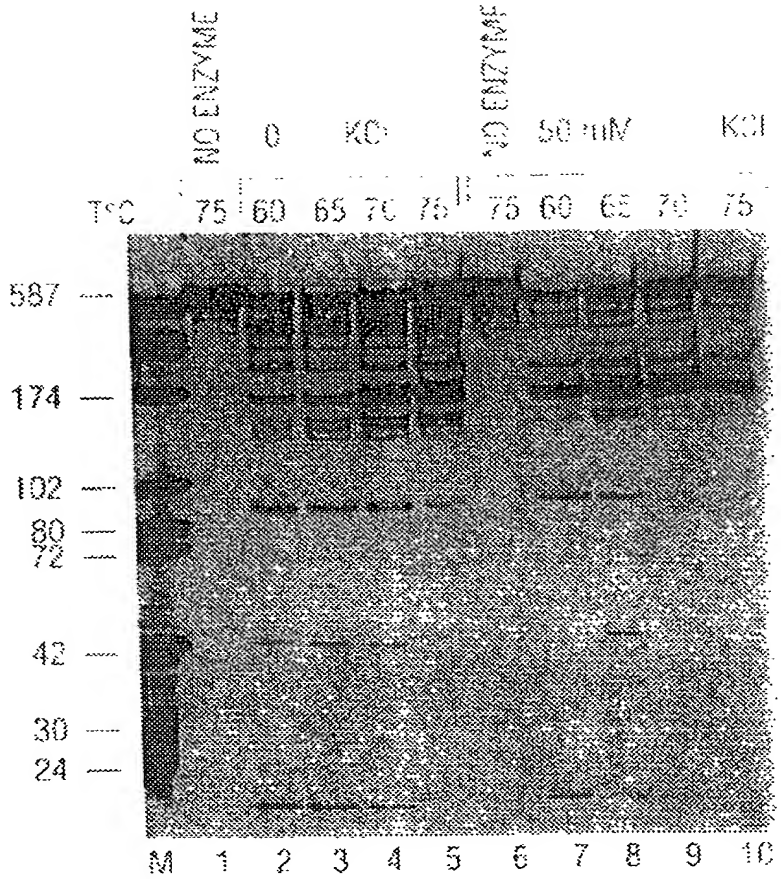

NO ENZYME
0
KCl
50 mM
KCl
75
60
65
75
75
60
75
587
174
102
80
72
43
30
24
M
1
2
3
4
5
6
7
8
9
10

FIG. 41

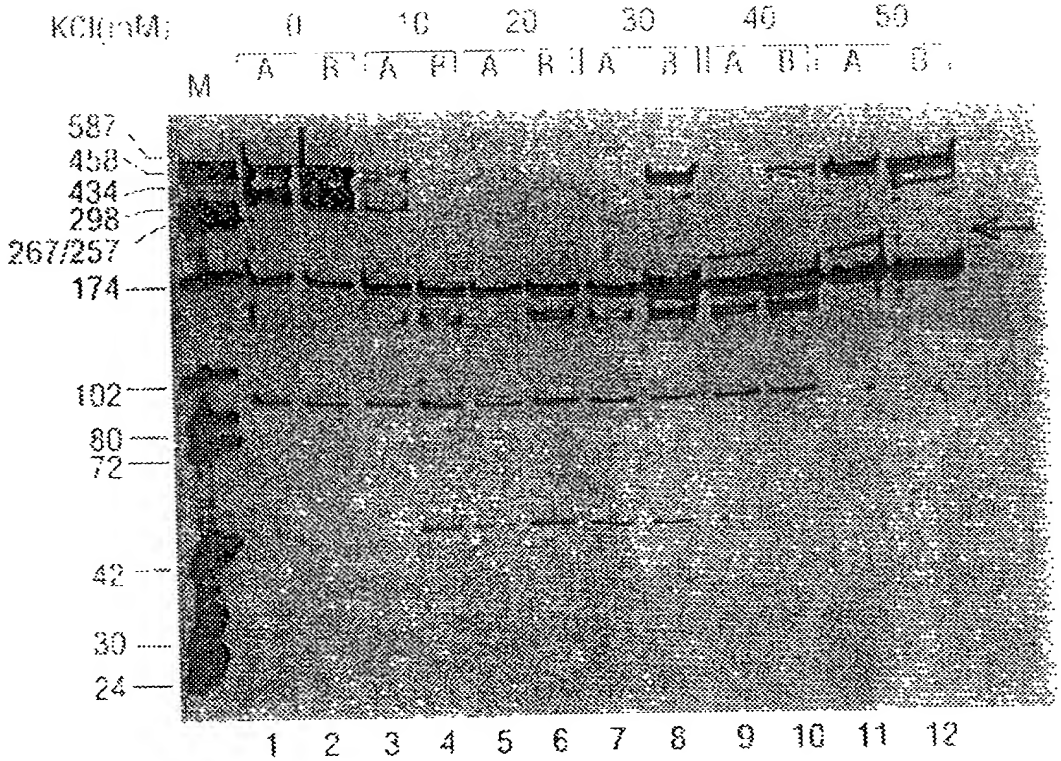

KCl(mM): 0 10 20 30 40 50
A B A B A B A B A B A B
M
587
458
434
298
267/257
174
102
80
72
42
30
24
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 42

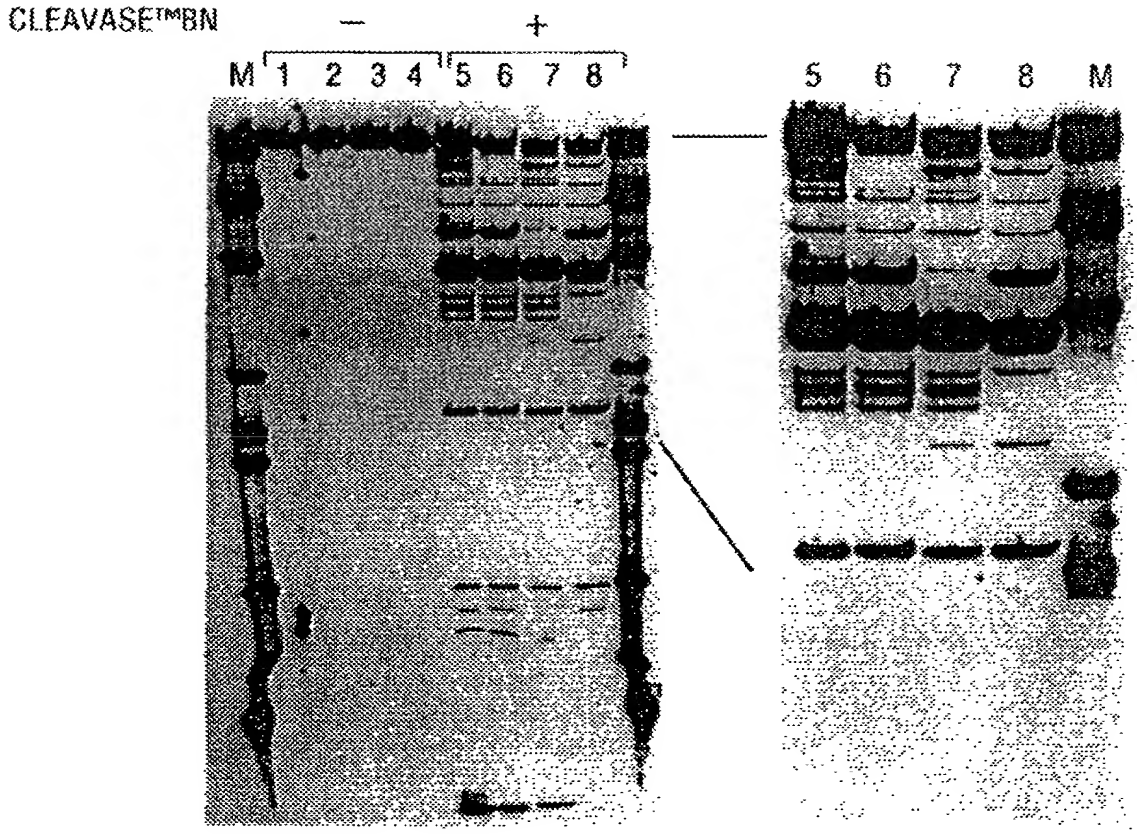


FIG. 43

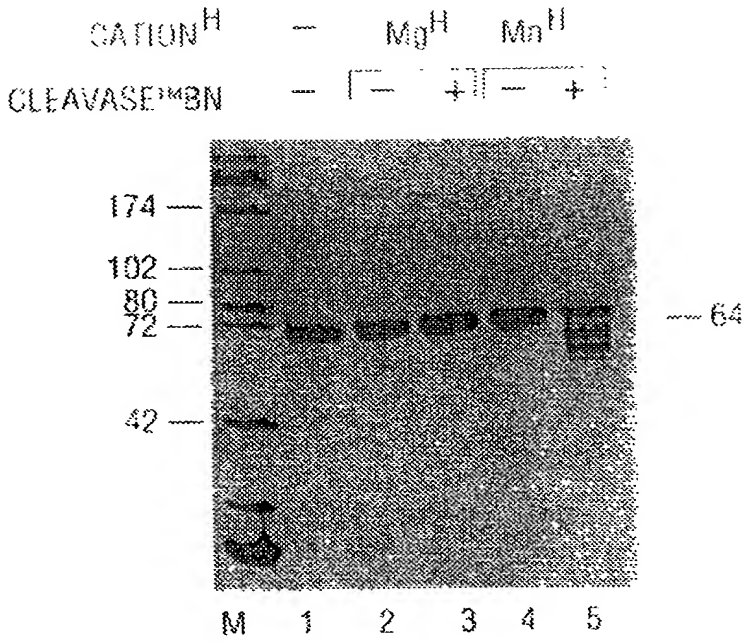


FIG. 44

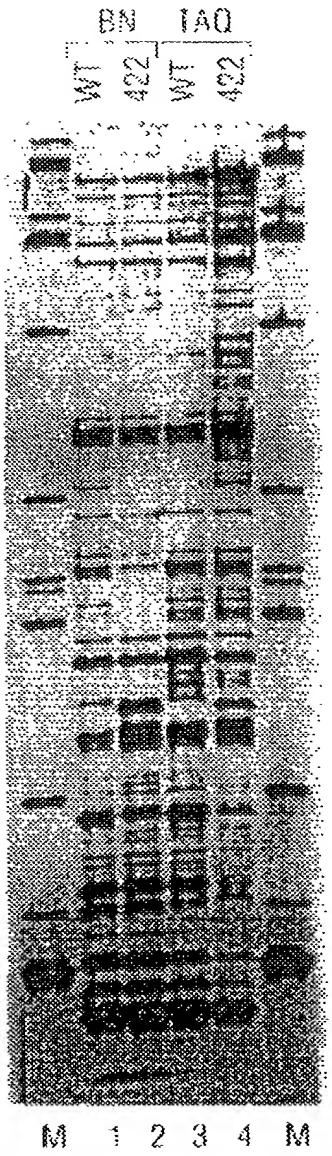


FIG. 45

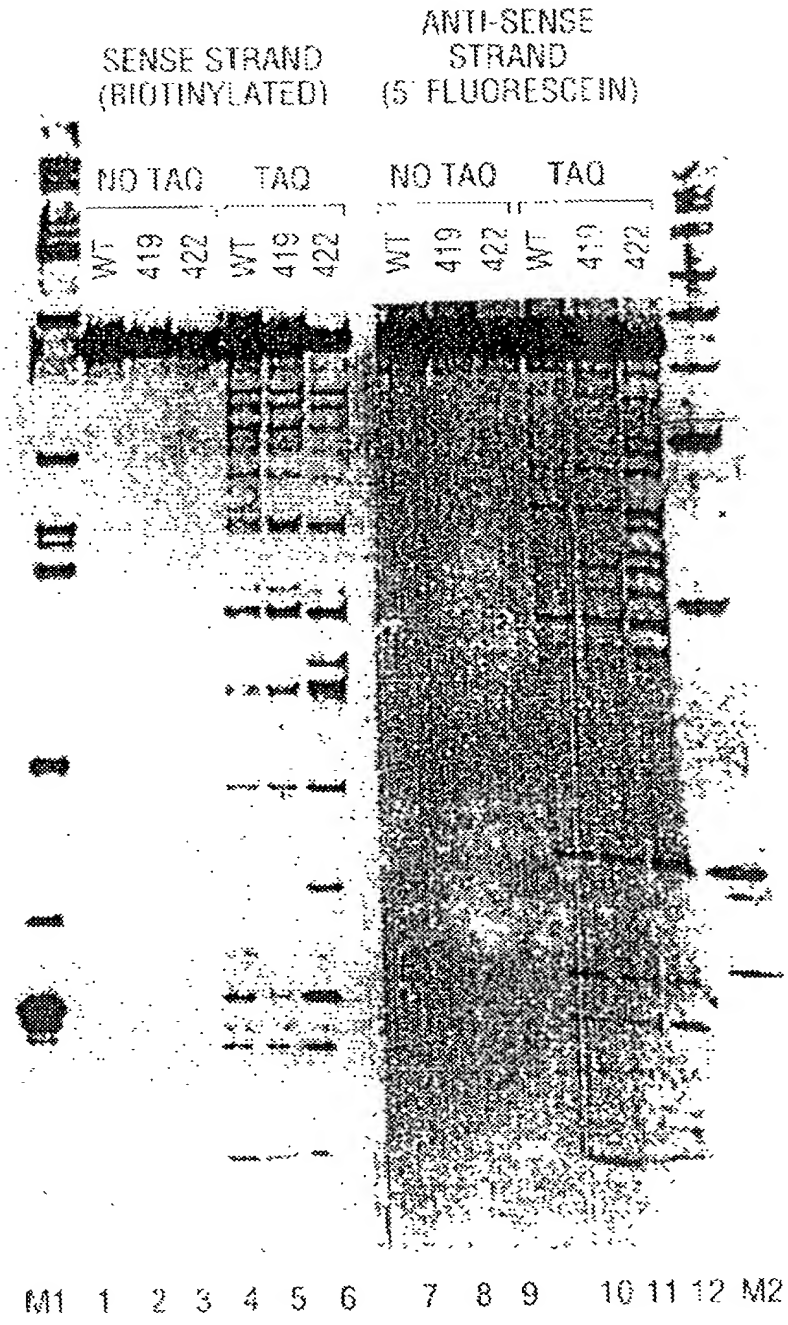

SENSE STRAND
(BIOTINYLATED)
ANTI-SENSE
STRAND
(5' FLUORESCEIN)
NO TAQ
TAQ
NO TAQ
TAQ
WT
419
422
WT
419
422
WT
419
422
WT
419
422
M1 1 2 3 4 5 6 7 8 9 10 11 12 M2

FIG. 46

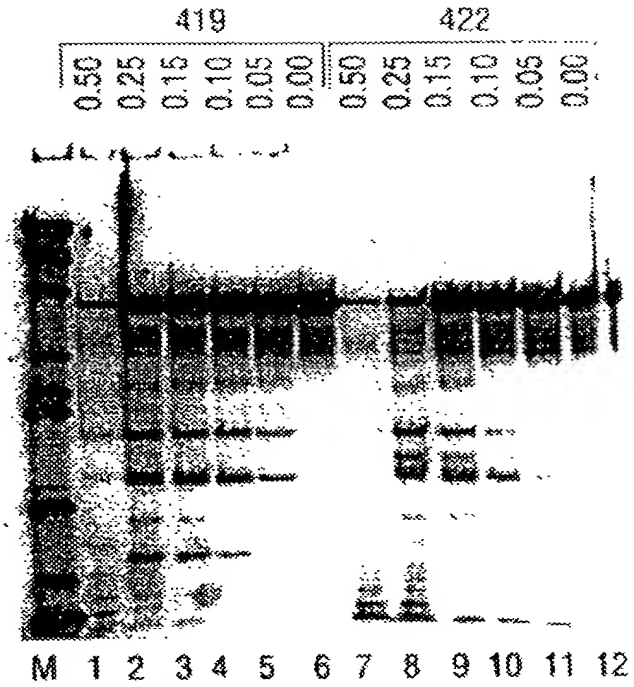

419
422
0.50
0.25
0.15
0.10
0.05
0.00
0.50
0.25
0.15
0.10
0.05
0.00
M 1 2 3 4 5 6 7 8 9 10 11 12

FIG. 47

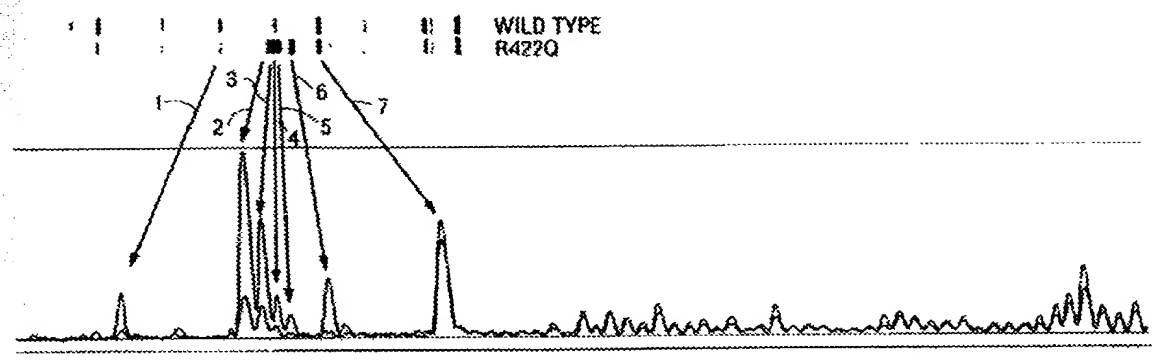


FIG. 48

50

L.100.8-1	5'GGCTGACAAGAAGGAAACTCGCTGAGACAGCAGGGACTTTCCACAAGGGG
(SEQ ID NO: 76)	3'CCGACTGTTCTTCCTTTGAGCGACTCTGTCGTCCCTGAAAGGTGTTCCCC
L.46.16-10	5'GGCTGACAAGAAGGAAACTCGCTGAGATAGCAGGGACTTTCCACAAGGGG
(SEQ ID NO: 77)	3'CCGACTGTTCTTCCTTTGAGCGACTCTATCGTCCCTGAAAGGTGTTCCCC
L.46.16-12	5'GGCTGACAAGAAGGAAACTCGCTGAGATAGCAGGGACTTTCCACAAGGGG
(SEQ ID NO: 78)	3'CCGACTGTTCTTCCTTTGAGCGACTCTATCGTCCCTGAAAGGTGTTCCCC
L19.16-3	5'GGCTGACAAGAAGGAAACTCGCTGAGACAGCAGGGACTTTCCACAAGGGG
(SEQ ID NO: 79)	3'CCGACTGTTCTTCCTTTGAGCGACTCTGTCGTCCCTGAAAGGTGTTCCCC
L.CEM/251	5'GGCTGACAAGAAGGAAACTCGCTGAAACAGCAGGGACTTTCCACAAGGGG
(SEQ ID NO: 80)	3'CCGACTGTTCTTCCTTTGAGCGACTTTGTCGTCCCTGAAAGGTGTTCCCC
L.36.8-3	5'GGCTGACAAGAAGGAAACTCGCTGAGACAGCAGGGACTTTCCACAAGGGG
(SEQ ID NO: 81)	3'CCGACTGTTCTTCCTTTGAGCGACTCTGTCGTCCCTGAAAGGTGTTCCCC

FIG. 49A

```
                                                                  100
L.100.8-1          ATGTTACGGGGAGGTACTGGGGAGGAGCCGGTCGGGAACGCCCACTCTCT
(SEQ ID NO: 76)    TACAATGCCCCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGTGAGAGA

L.46.16-10         ATGTTATGGGGAGG----------AGCCGGTCGGGAACACCCACTTTCT
(SEQ ID NO: 77)    TACAATACCCCTCC----------TCGGCCAGCCCTTGTGGGTGAAAGA

L.46.16-12         ATGTTATGGGGAGG----------AGCCGGTCGGGAACACCCACTTTCT
(SEQ ID NO: 78)    TACAATACCCCTCC----------TCGGCCAGCCCTTGTGGGTGAAAGA

L19.16-3           ATGTTACGGGGAGGTACTGGGGAGGAGCCGGTCGGGAACGCCCCCTCTCT
(SEQ ID NO: 19)    TACAATGCCCCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGGGAGAGA

L.CEM/251          ATGTTACGGGGAGGTACTGGGAAGGAGCCGGTCGGGAACGCCCACTTTCT
(SEQ ID NO: 80)    TACAATGCCCCTCCATGACCCTTCCTCGGCCAGCCCTTGCGGGTGAAAGA

L.36.8-3           ATGTTACGGAGAGGTACTGGGGAGGAGCCGGTCGGGAACGCCCACTCTCT
(SEQ ID NO: 81)    TACAATGCCTCTCCATGACCCCTCCTCGGCCAGCCCTTGCGGGTGAGAGA
```

FIG. 49B

		150
L.100.8-1	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGGA 3'ACTACATATTTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT	
L.46.16-10	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGGA 3'ACTACATATTTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT	
L.46.16-12	5'TGGTGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGGA 3'ACCACATATTTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT	
L.19.16-3	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGGA 3'ACTACATATTTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT	
L.CEM/251	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGGA 3'ACTACATATTTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT	
L.36.8-3	5'TGATGTATAAATATCACTGCATTTCGCTCTGTATTCAGTCGCTCTGCGGA 3'ACTACATATTTATAGTGACGTAAAGCGAGACATAAGTCAGCGAGACGCCT	

FIG. 49C

200

L.100.8-1	GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
	CTCCGACCGTCTAACTCGGGACCCTCCAAGAGAGGTCGTGATCGTCCATC
L.46.16-10	GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGCTAG
	CTCCGACCGTCTAACTCGGGACCCTCCAAGAGAGGTCGTGATCGTCCATC
L.46.16-12	GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
	CTCCGACCGTCTAACTCGGGACCCTCCAAGAGAGGTCGTGATCGTCCATC
L.19.16-3	GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
	CTCCGACCGTCTAACTCGGGACCCTCCAAGAGAGGTCGTGATCGTCCATC
L.CEM/251	GAGGCTGGCAGATTGAGCCCTGGGAGGTTCTCTCCAGCACTAGCAGGTAG
	CTCCGACCGTCTAACTCGGGACCCTCCAAGAGAGGTCGTGATCGTCCATC
L.36.8-3	GAGGCTGGCAGATTGAGCCCTAGGAGGTTCTCTCCAGCACTAGCAGGTAG
	CTCCGACCGTCTAACTCGGGATCCTCCAAGAGAGGTCGTGATCGTCCATC

FIG. 49D

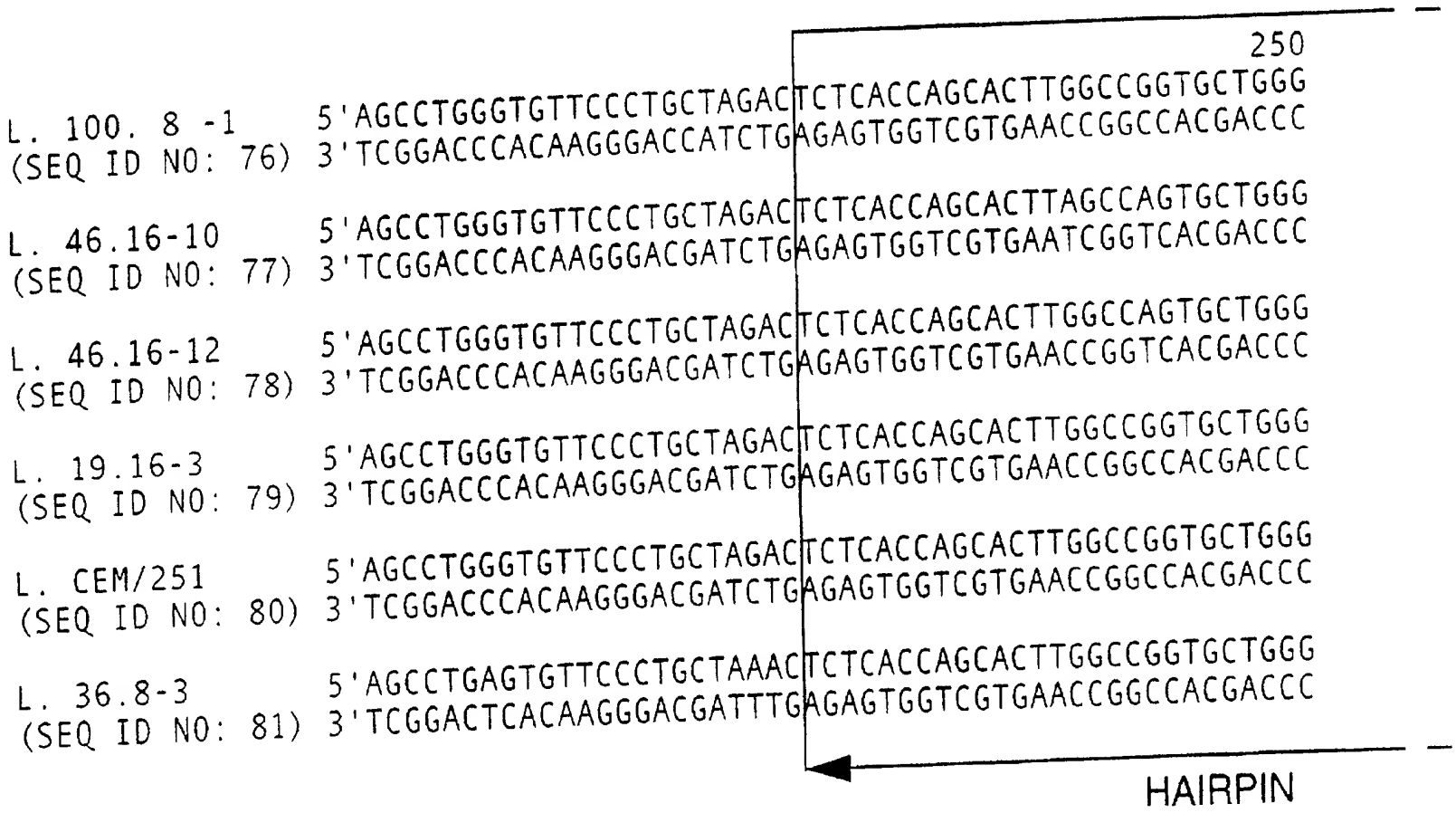

250
L. 100. 8 -1
(SEQ ID NO: 76)
5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG
3'TCGGACCCACAAGGGACCATCTGAGAGTGGTCGTGAACCGGCCACGACCC
L. 46.16-10
(SEQ ID NO: 77)
5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTAGCCAGTGCTGGG
3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAATCGGTCACGACCC
L. 46.16-12
(SEQ ID NO: 78)
5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCAGTGCTGGG
3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAACCGGTCACGACCC
L. 19.16-3
(SEQ ID NO: 79)
5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG
3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAACCGGCCACGACCC
L. CEM/251
(SEQ ID NO: 80)
5'AGCCTGGGTGTTCCCTGCTAGACTCTCACCAGCACTTGGCCGGTGCTGGG
3'TCGGACCCACAAGGGACGATCTGAGAGTGGTCGTGAACCGGCCACGACCC
L. 36.8-3
(SEQ ID NO: 81)
5'AGCCTGAGTGTTCCCTGCTAAACTCTCACCAGCACTTGGCCGGTGCTGGG
3'TCGGACTCACAAGGGACGATTTGAGAGTGGTCGTGAACCGGCCACGACCC
HAIRPIN

FIG. 49E

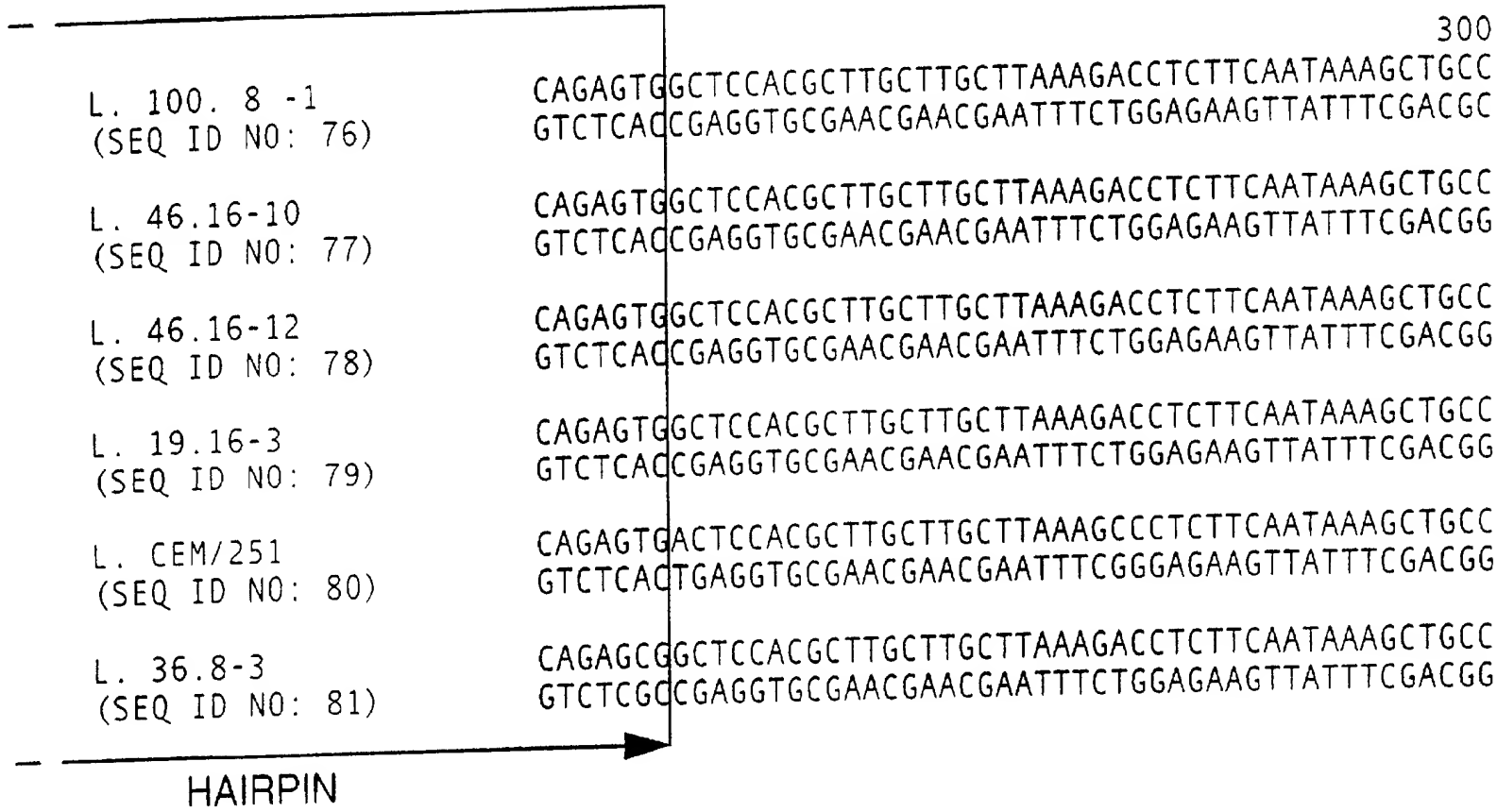

300
L. 100. 8 -1
(SEQ ID NO: 76)
CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
GTCTCACCGAGGTGCGAACGAACGAATTTCTGGAGAAGTTATTTCGACGC
L. 46.16-10
(SEQ ID NO: 77)
CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
GTCTCACCGAGGTGCGAACGAACGAATTTCTGGAGAAGTTATTTCGACGG
L. 46.16-12
(SEQ ID NO: 78)
CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
GTCTCACCGAGGTGCGAACGAACGAATTTCTGGAGAAGTTATTTCGACGG
L. 19.16-3
(SEQ ID NO: 79)
CAGAGTGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
GTCTCACCGAGGTGCGAACGAACGAATTTCTGGAGAAGTTATTTCGACGG
L. CEM/251
(SEQ ID NO: 80)
CAGAGTGACTCCACGCTTGCTTGCTTAAAGCCCTCTTCAATAAAGCTGCC
GTCTCACTGAGGTGCGAACGAACGAATTTCGGGAGAAGTTATTTCGACGG
L. 36.8-3
(SEQ ID NO: 81)
CAGAGCGGCTCCACGCTTGCTTGCTTAAAGACCTCTTCAATAAAGCTGCC
GTCTCGCCGAGGTGCGAACGAACGAATTTCTGGAGAAGTTATTTCGACGG
HAIRPIN

FIG. 49F

```
                                                                  350
L.100.8-1       5'ATTTTAGAAGTAGGCCAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCCTG  G 3'
                3'TAAAATCTTCATCCGGTCACACACAAGGGTAGAGAGGATCGGCGGCGGAC  C 5'

L.46,16-10      5'ATTTTAGAAGTAAGCCAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCCTG  G 3'
                3'TAAAATCTTCATTCGGTCACACACAAGGGTAGAGAGGATCGGCGGCGGAC  C 5'

L.46.16-12      5'ATTTTAGAAGTAAGCCAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCCTG  G 3'
                3'TAAAATCTTCATTCGGTCACACACAAGGGTAGAGAGGATCGGCGGCGGAC  C 5'

L.19.16-3       5'ATTTTAGAAGTAGGCTAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCCTG  G 3'
                3'TAAAATCTTCATCCGATCACACACAAGGGTAGAGAGGATCGGCGGCGGAC  C 5'

L.CEM/251       5'ATTTTAGAAGTAAGCTAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCCTG  G 3'
                3'TAAAATCTTCATTCGATCACACACAAGGGTAGAGAGGATCGGCGGCGGAC  C 5'

L.36.8-3        5'ATTTTAGAAGTAGGCTAGTGTGTGTTCCCATCTCTCCTAGCCGCCGCCTG  G 3'
                3'TAAAATCTTCATCCGATCACACACAAGGGTAGAGAGGATCGGCGGCGGAC  C 5'
```

FIG. 49G

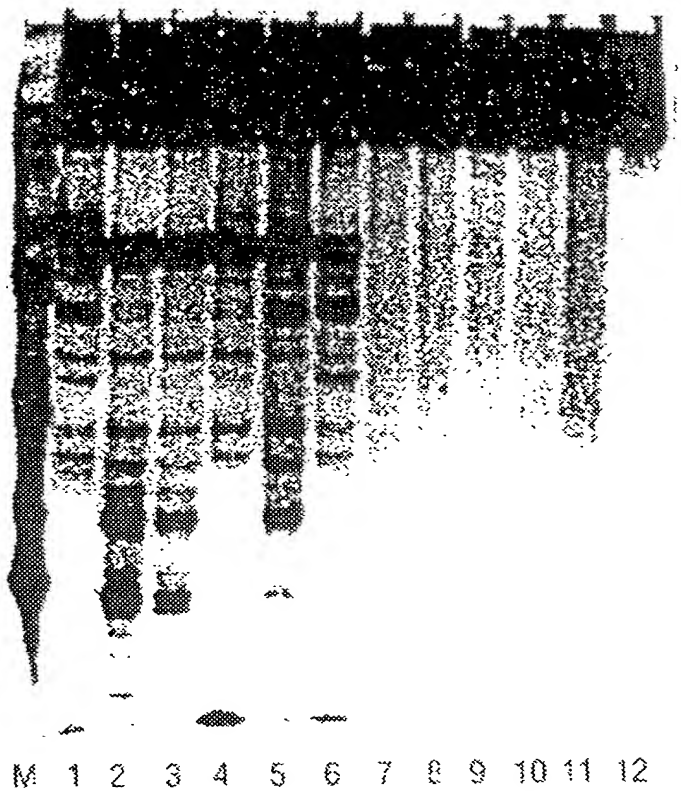


FIG. 50

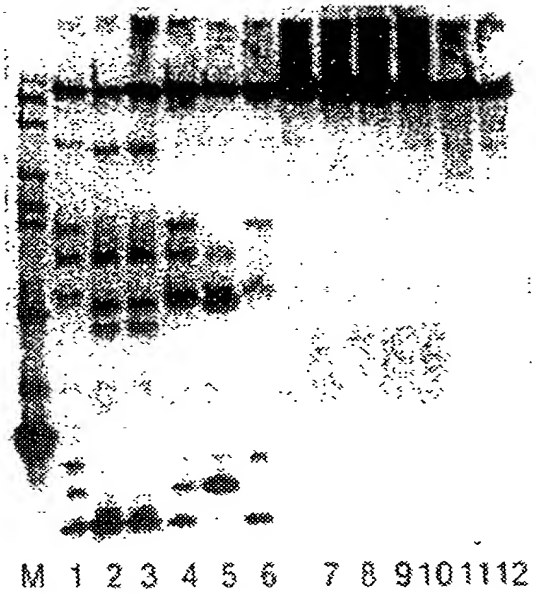


FIG. 51

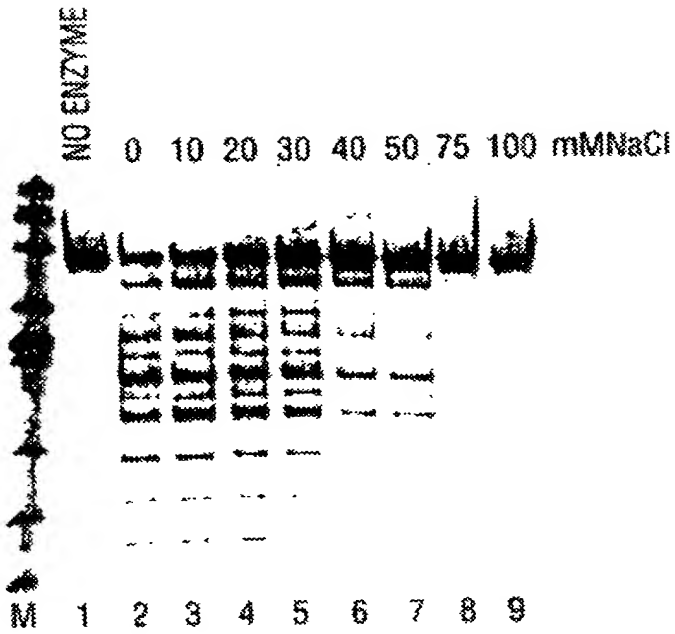


FIG. 52

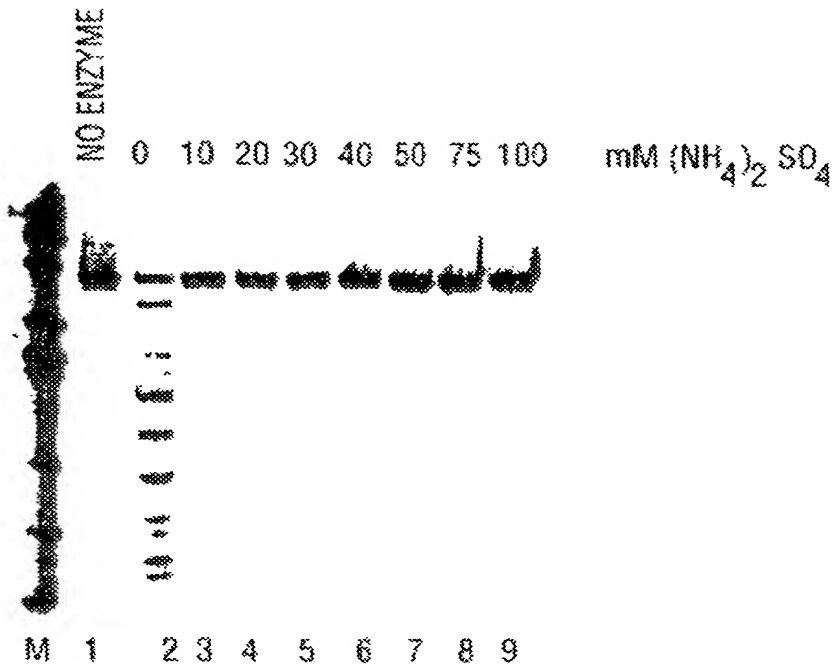


FIG. 53

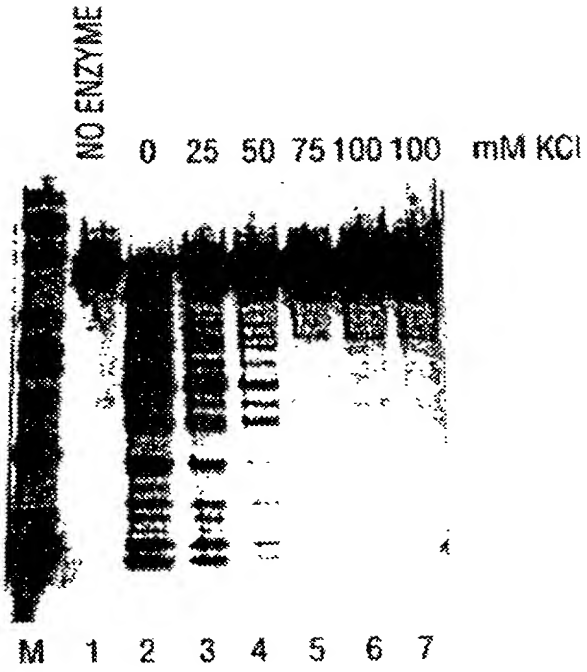


FIG. 54

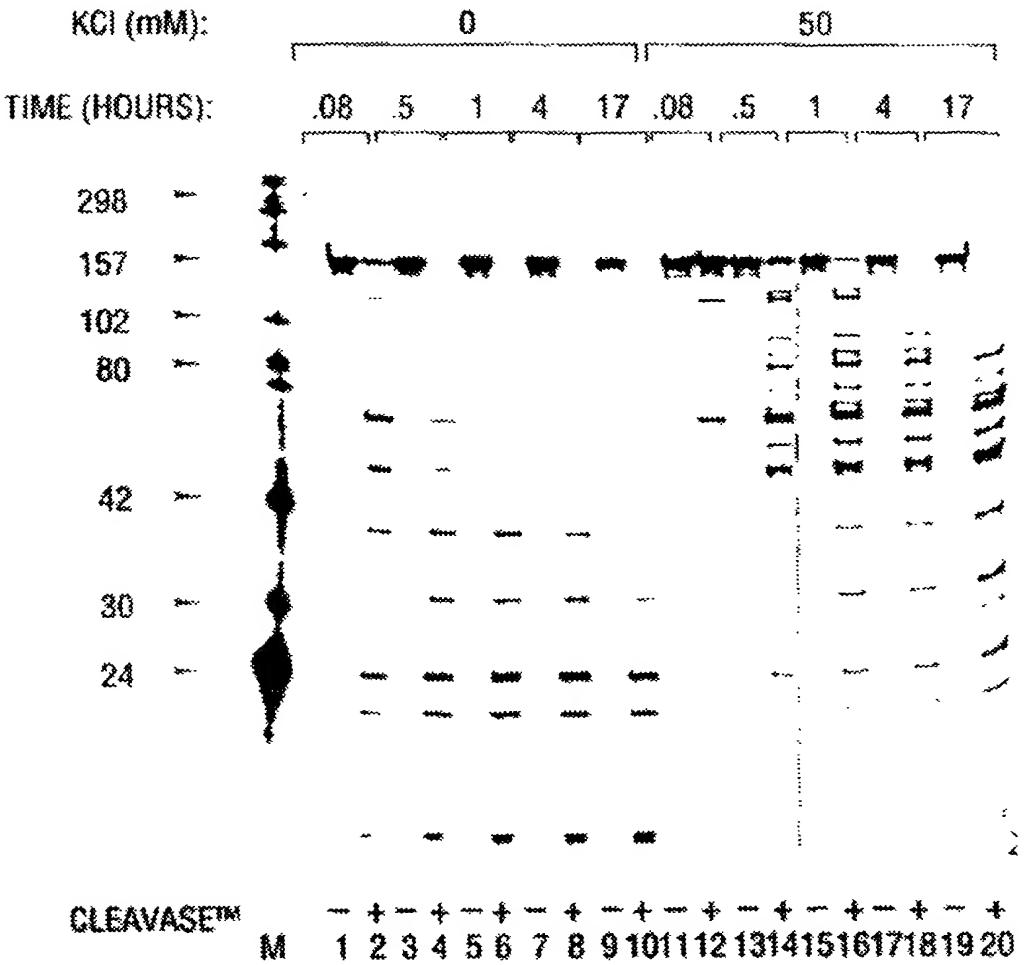

KCl (mM):
0
50
TIME (HOURS):
.08 .5 1 4 17 .08 .5 1 4 17
298
157
102
80
42
30
24
CLEAVASE™
M
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

FIG. 55

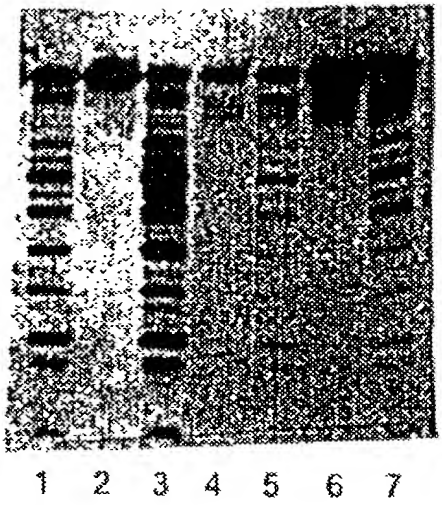


FIG. 56

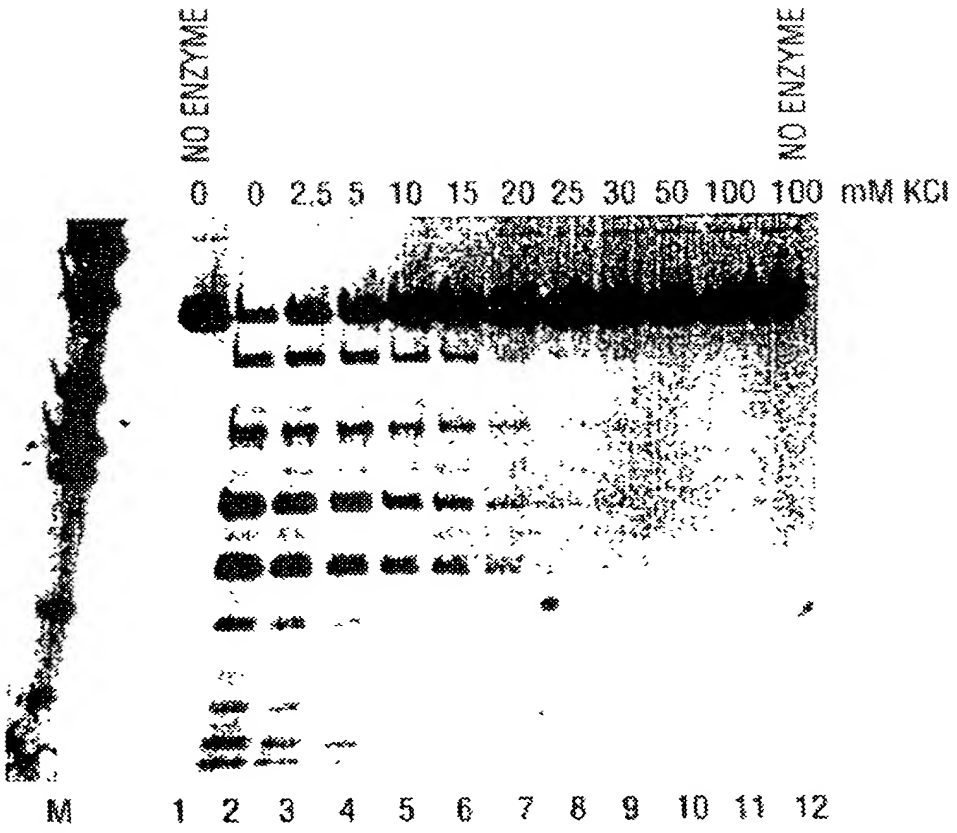

NO ENZYME
NO ENZYME
0 0 2.5 5 10 15 20 25 30 50 100 100 mM KCl
M 1 2 3 4 5 6 7 8 9 10 11 12

FIG. 57

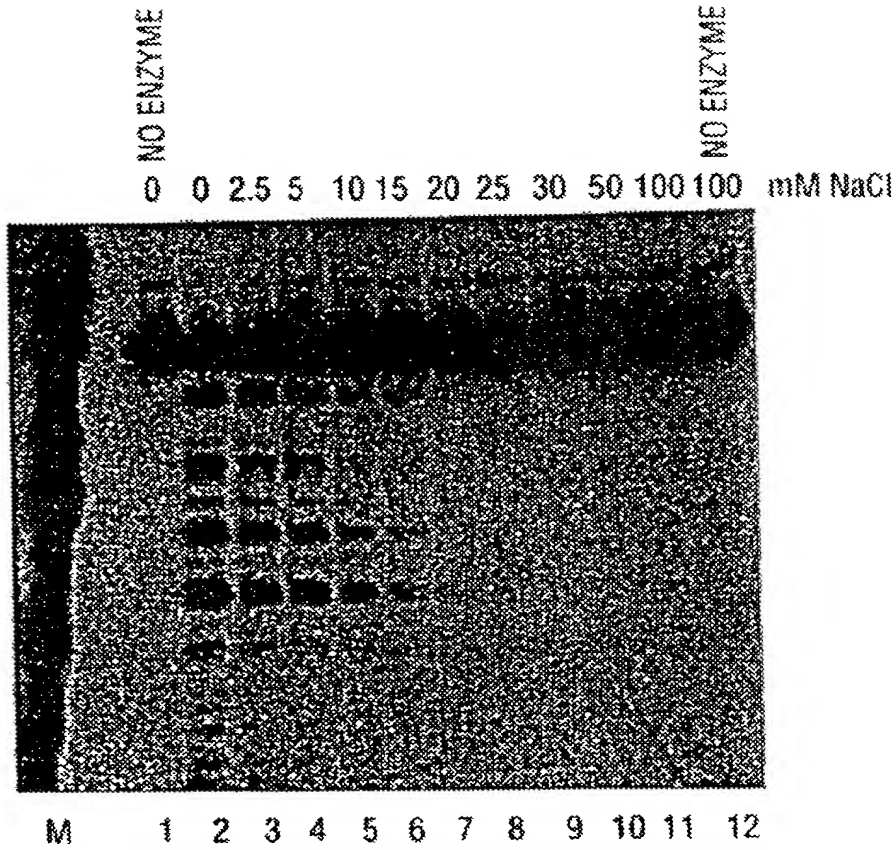

NO ENZYME
NO ENZYME
0 0 2.5 5 10 15 20 25 30 50 100 100 mM NaCl
M 1 2 3 4 5 6 7 8 9 10 11 12

FIG. 58

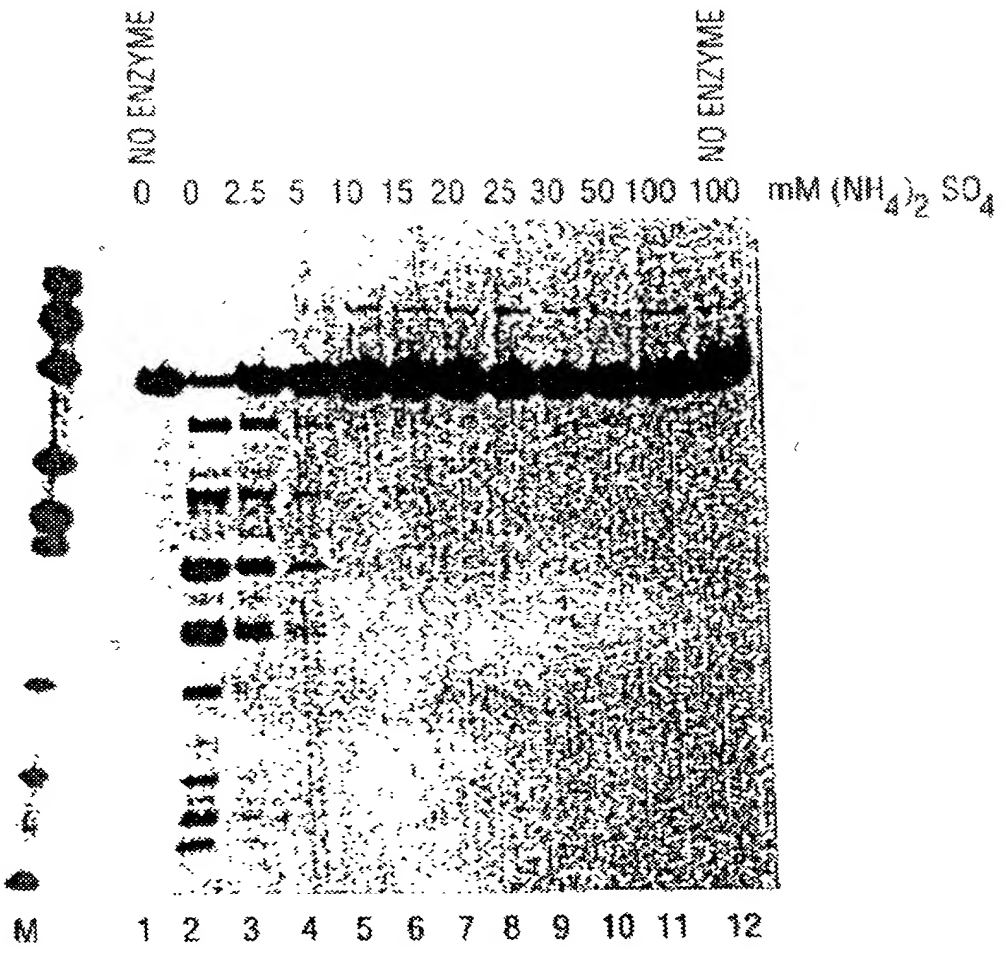

NO ENZYME
NO ENZYME
0 0 2.5 5 10 15 20 25 30 50 100 100 mM $(NH_4)_2$ SO_4
M 1 2 3 4 5 6 7 8 9 10 11 12

FIG. 59

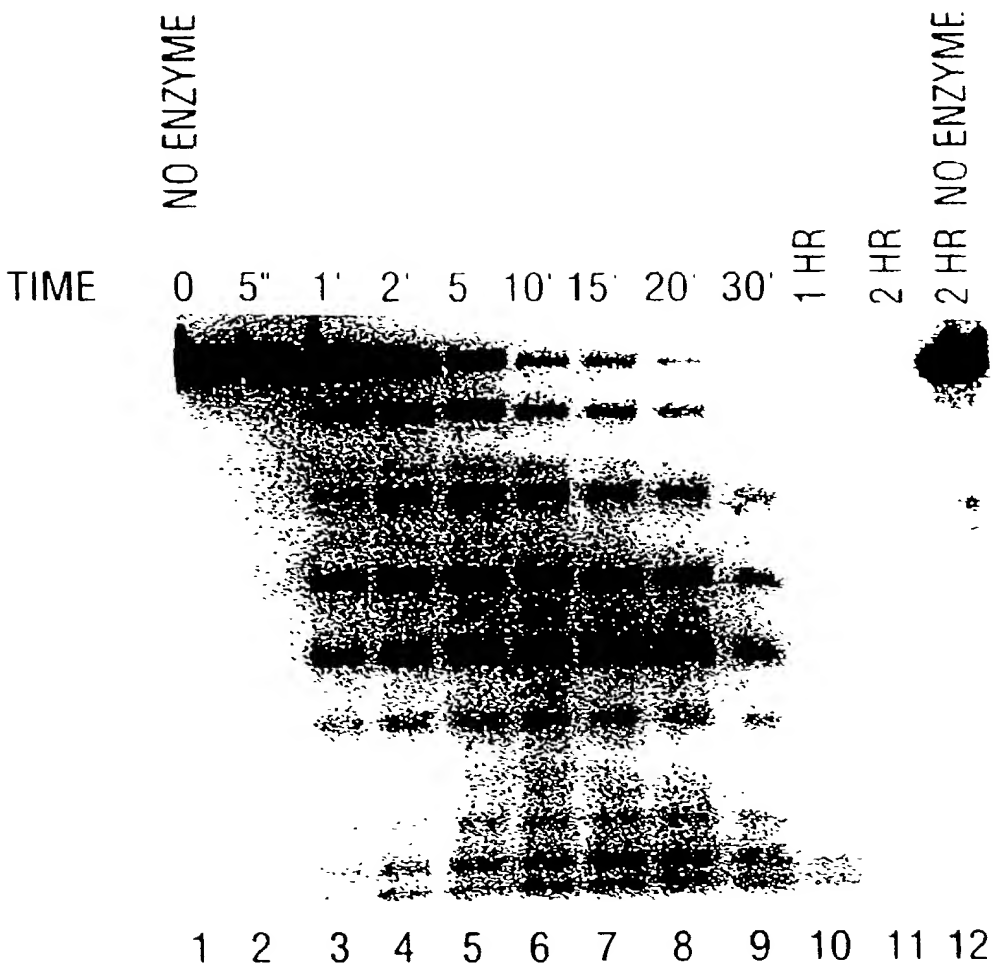

NO ENZYME
TIME
0
5"
1'
2'
5
10'
15'
20'
30'
1 HR
2 HR
2 HR
NO ENZYME
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 60

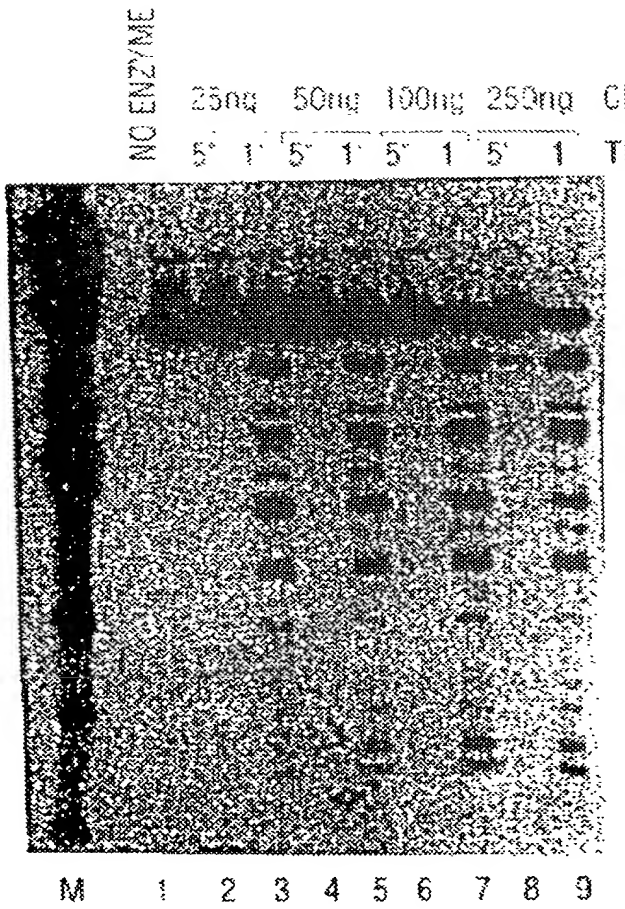

NO ENZYME
25ng 50ng 100ng 250ng CLEAVASE™BN
5' 1' 5' 1' 5' 1' 5' 1' TIME
M 1 2 3 4 5 6 7 8 9

FIG. 61

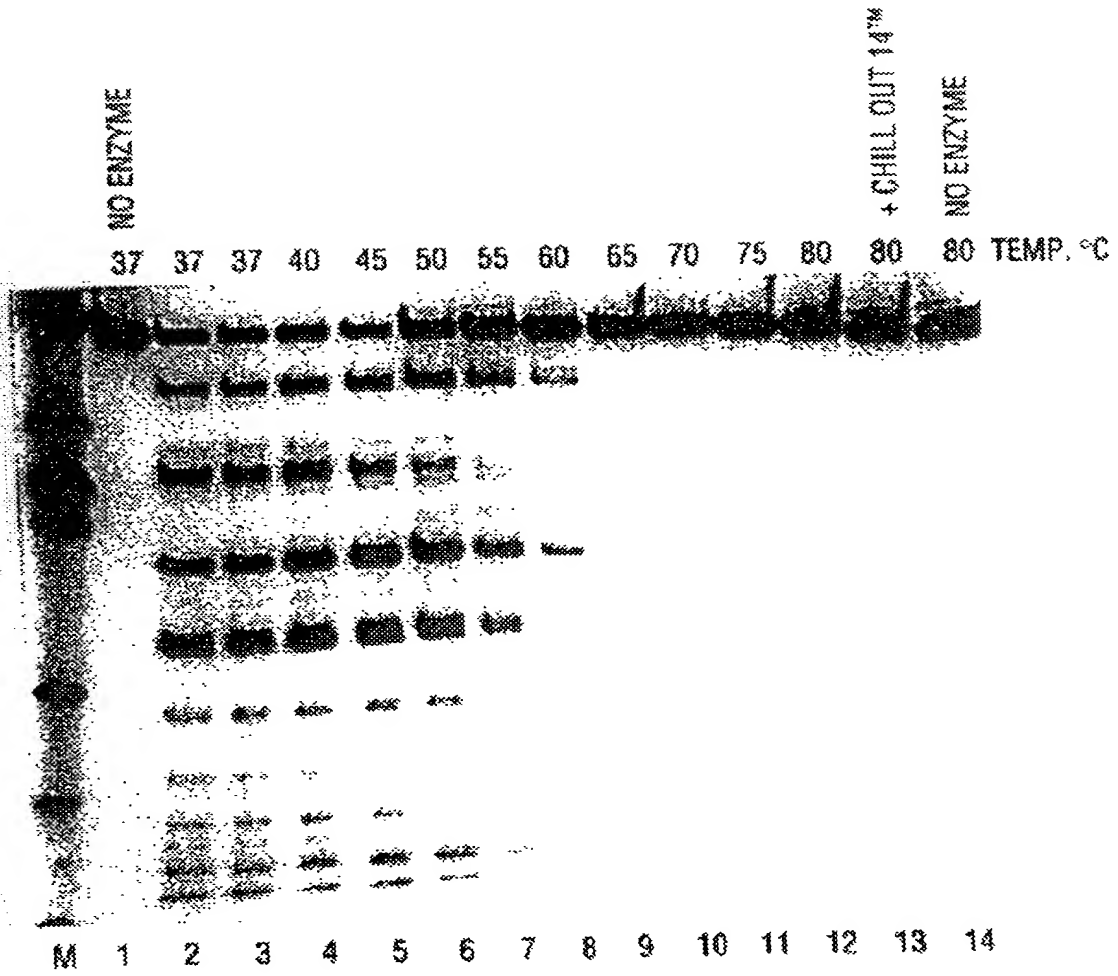

NO ENZYME
+ CHILL OUT 14™
NO ENZYME
37 37 37 40 45 50 55 60 65 70 75 80 80 80 TEMP. °C
M 1 2 3 4 5 6 7 8 9 10 11 12 13 14

FIG. 62

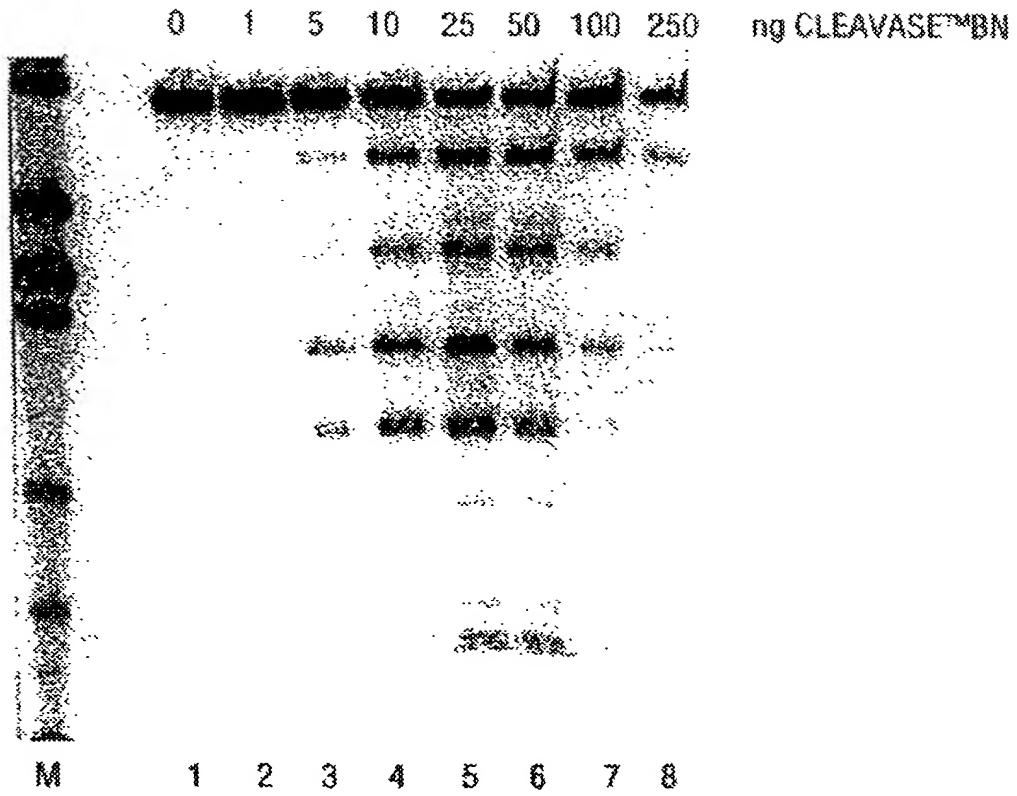


FIG. 63

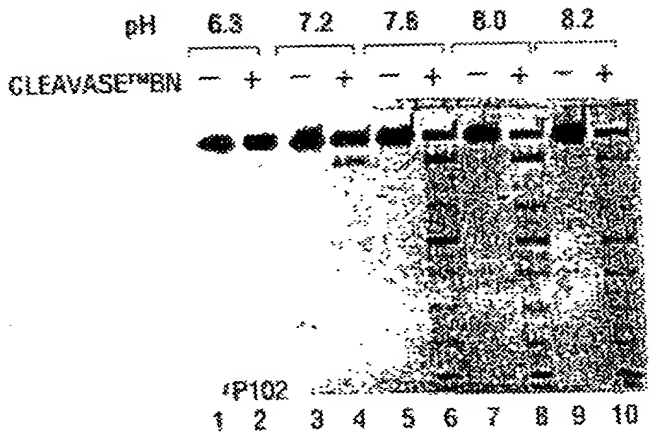


FIG. 64A

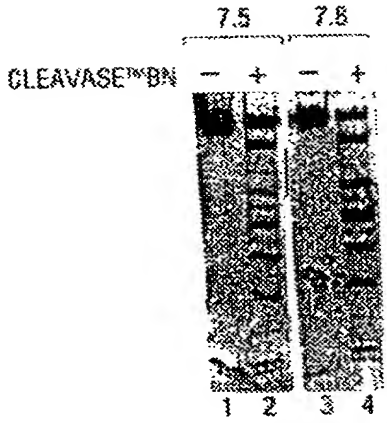


FIG. 64B

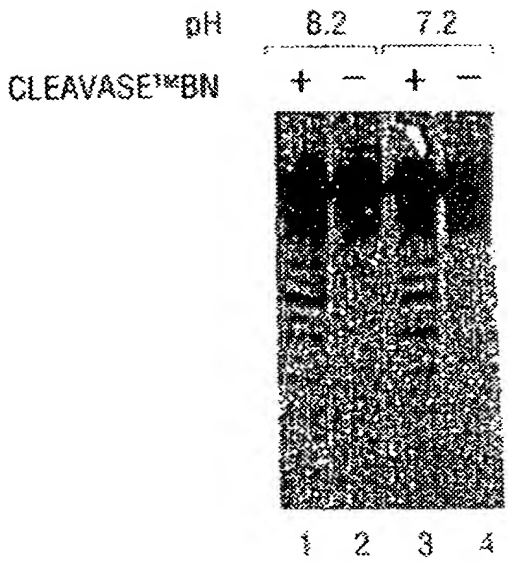


FIG. 65A

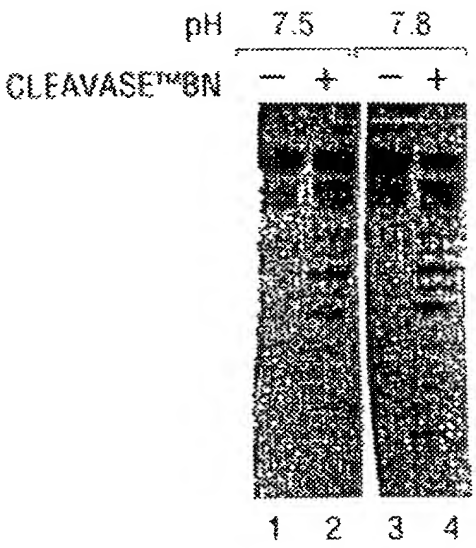


FIG. 65B

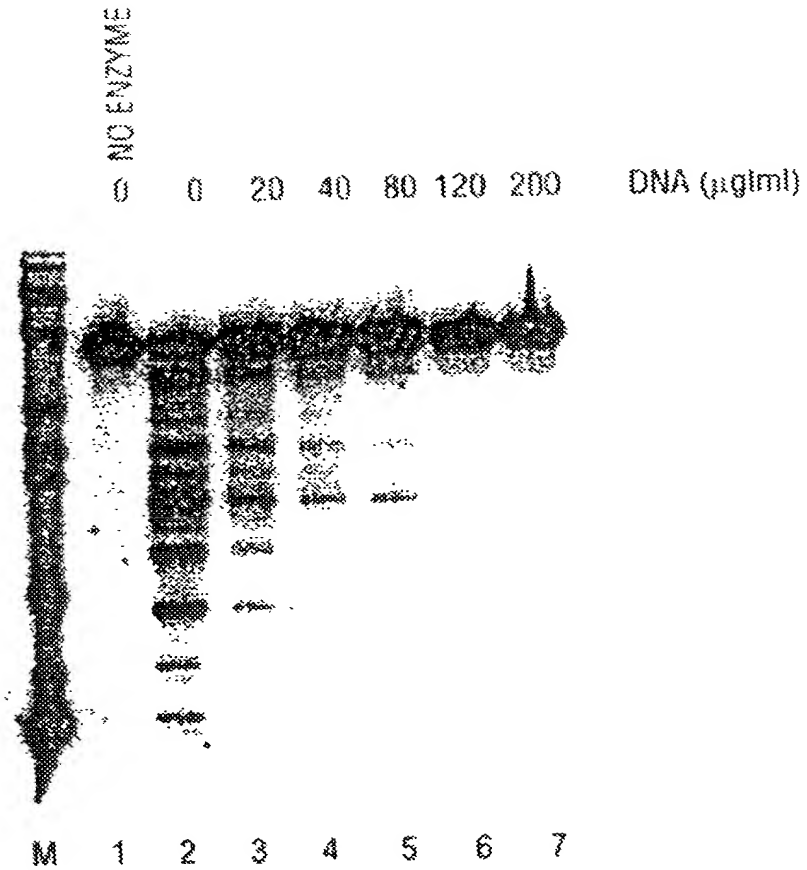


FIG. 66

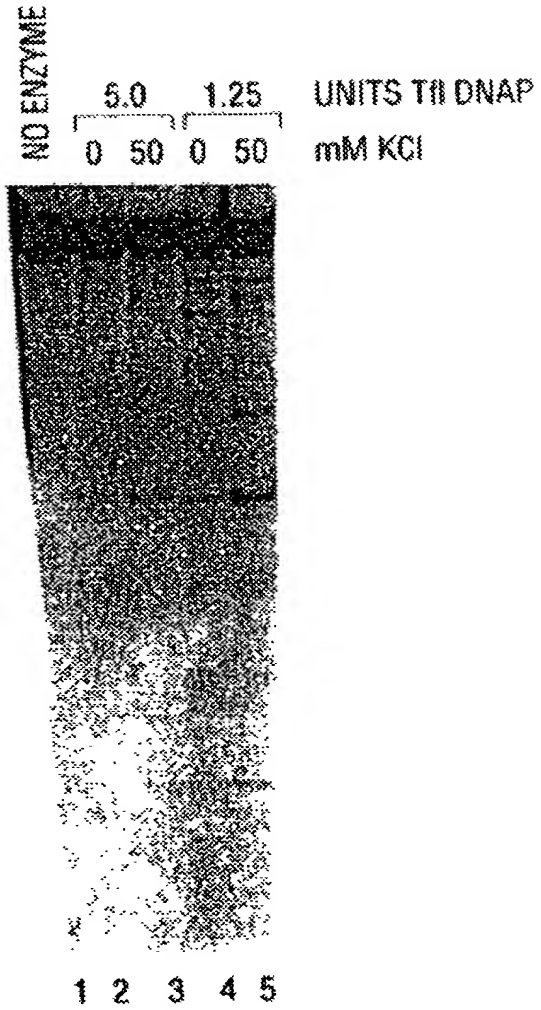


FIG. 67

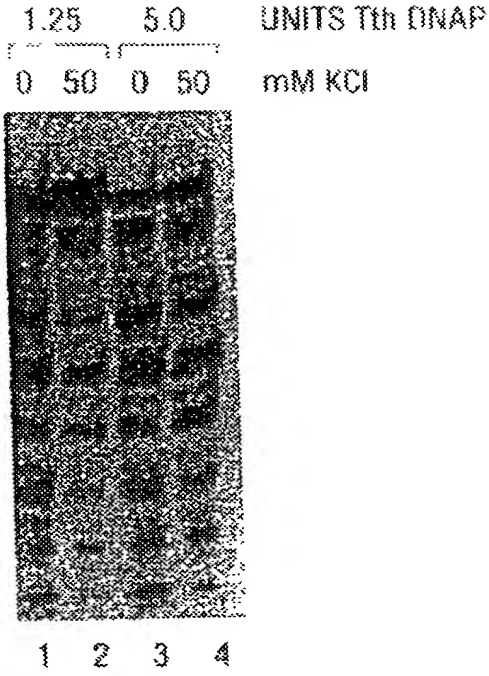


FIG. 68

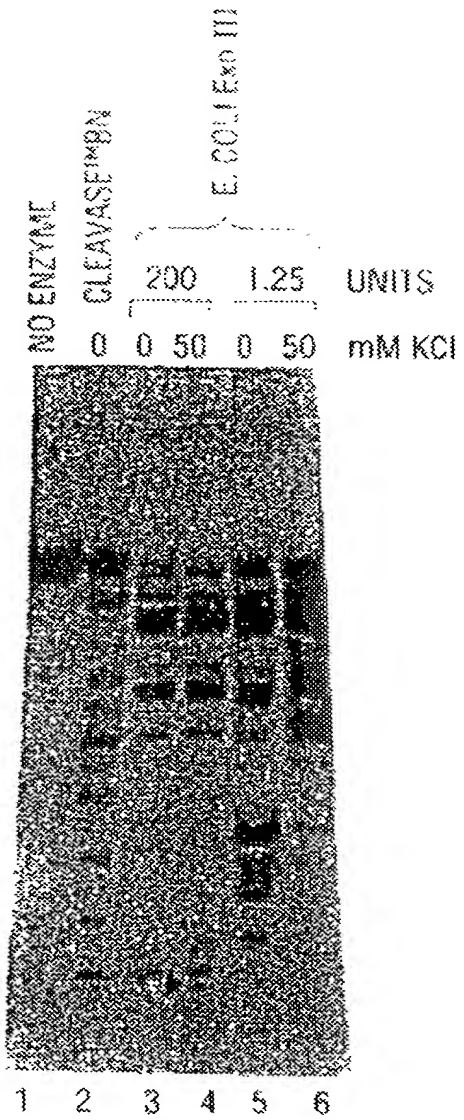

NO ENZYME
CLEAVASE™BN
E. COLI Exo III
200
1.25
UNITS
0 0 50 0 50
mM KCl
1 2 3 4 5 6

FIG. 69

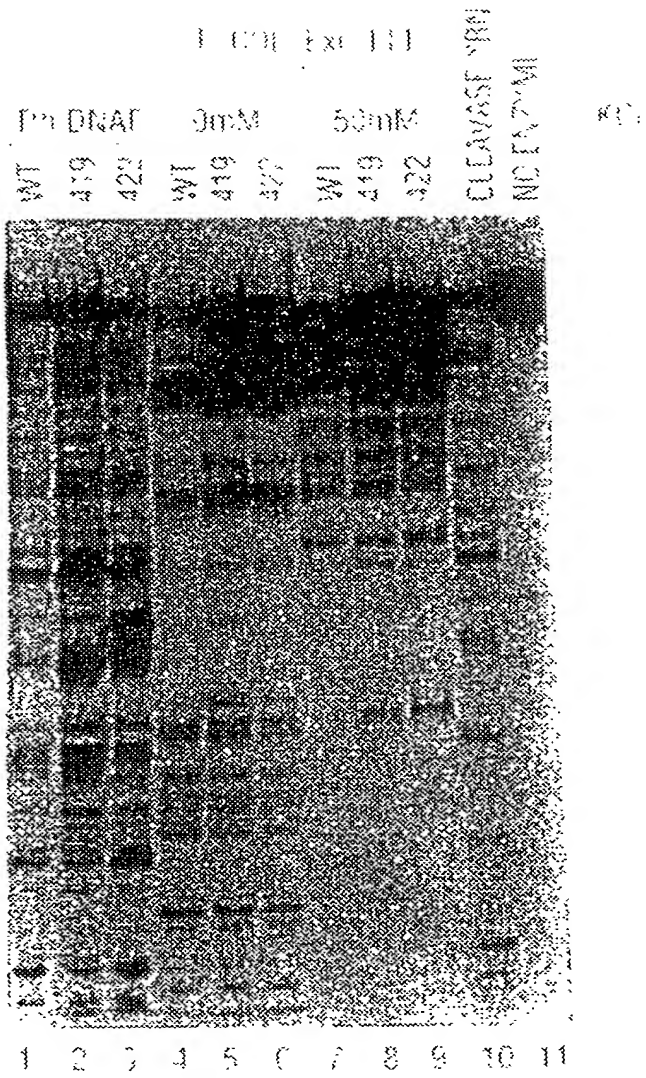


FIG. 70

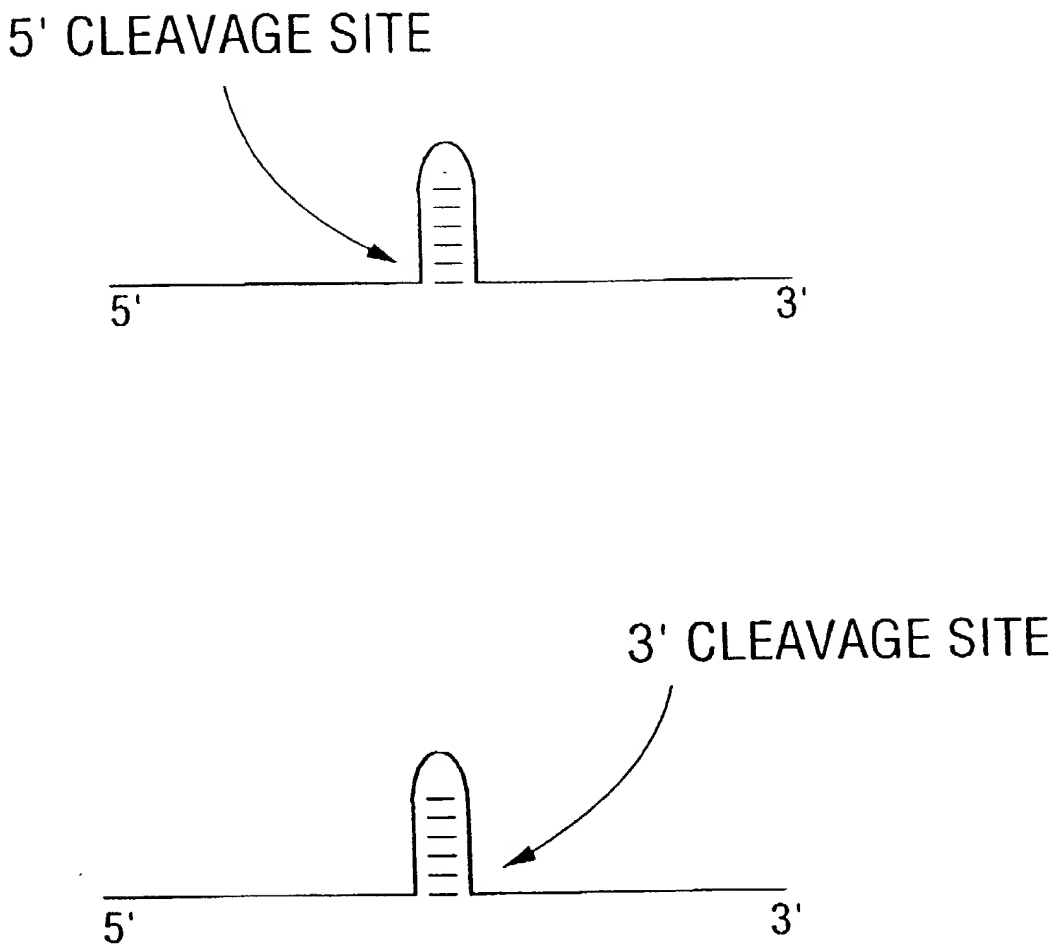


FIG. 71

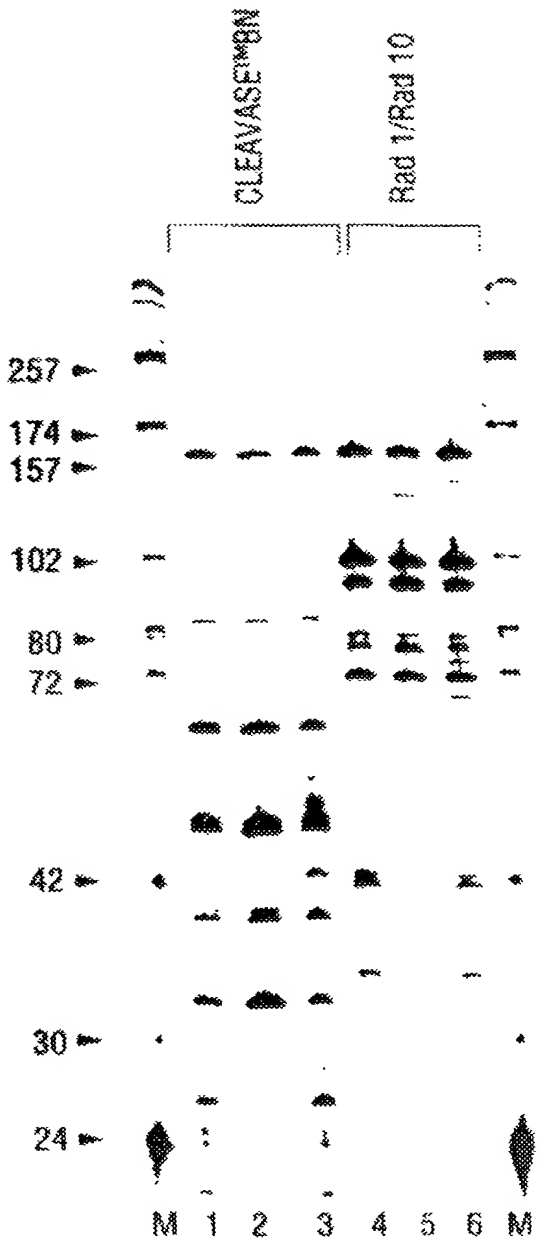


FIG. 72

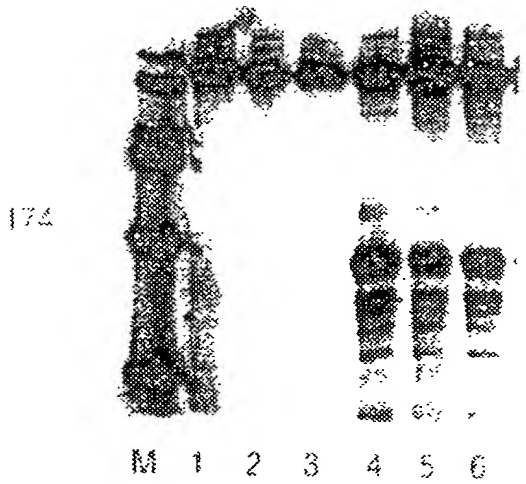


FIG. 73

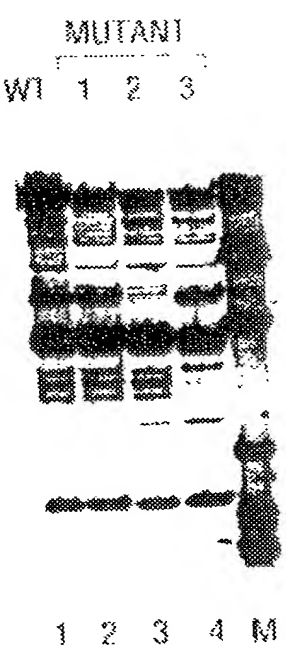


FIG. 74A

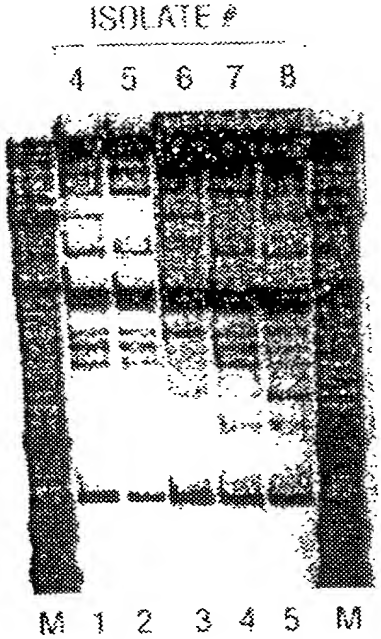


FIG. 74B

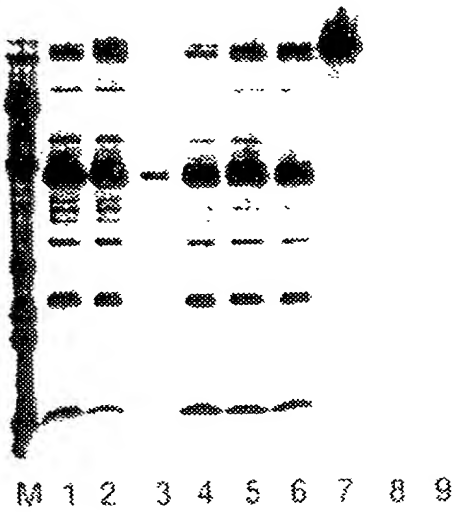


FIG. 75

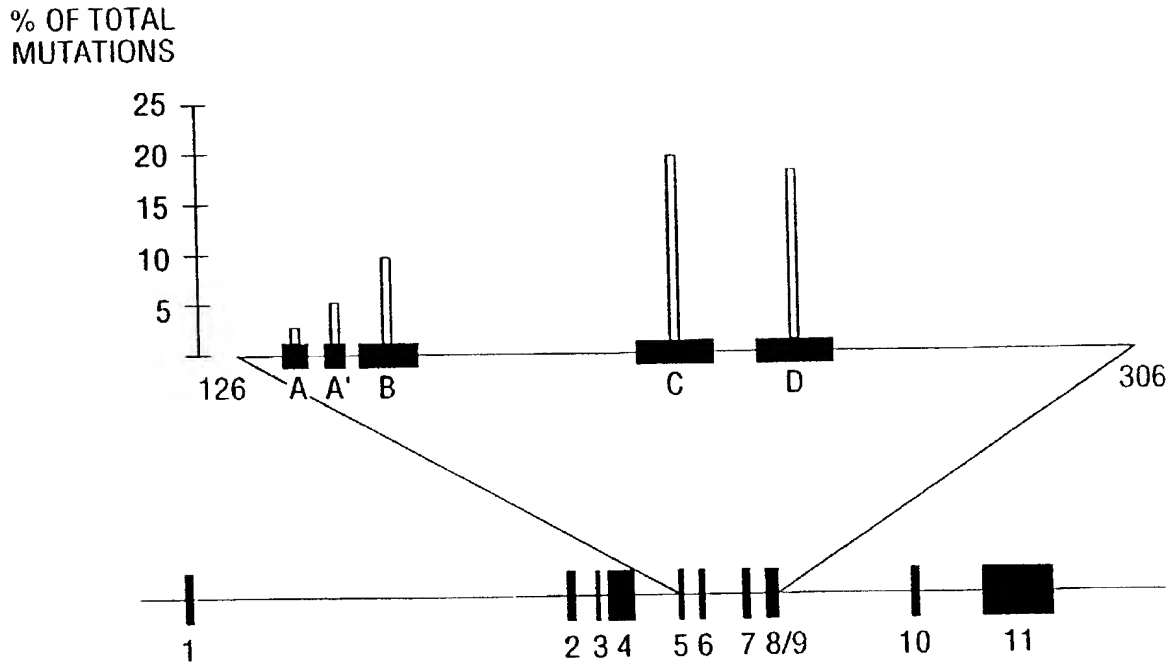


FIG. 76

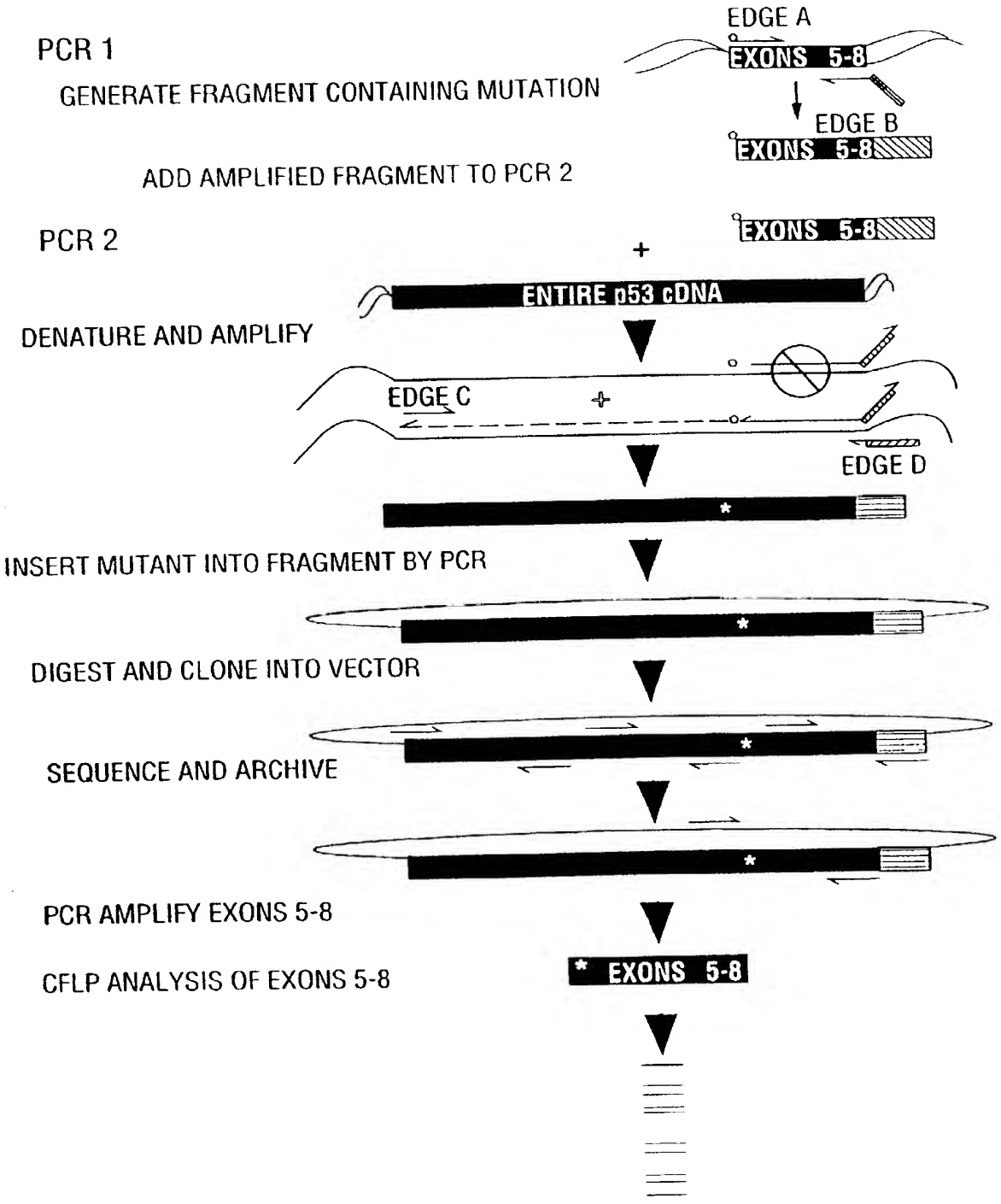

PCR 1
GENERATE FRAGMENT CONTAINING MUTATION
EDGE A
EXONS 5-8
EDGE B
EXONS 5-8
ADD AMPLIFIED FRAGMENT TO PCR 2
PCR 2
EXONS 5-8
+
ENTIRE p53 cDNA
DENATURE AND AMPLIFY
EDGE C
EDGE D
INSERT MUTANT INTO FRAGMENT BY PCR
DIGEST AND CLONE INTO VECTOR
SEQUENCE AND ARCHIVE
PCR AMPLIFY EXONS 5-8
CFLP ANALYSIS OF EXONS 5-8
* EXONS 5-8

FIG. 77

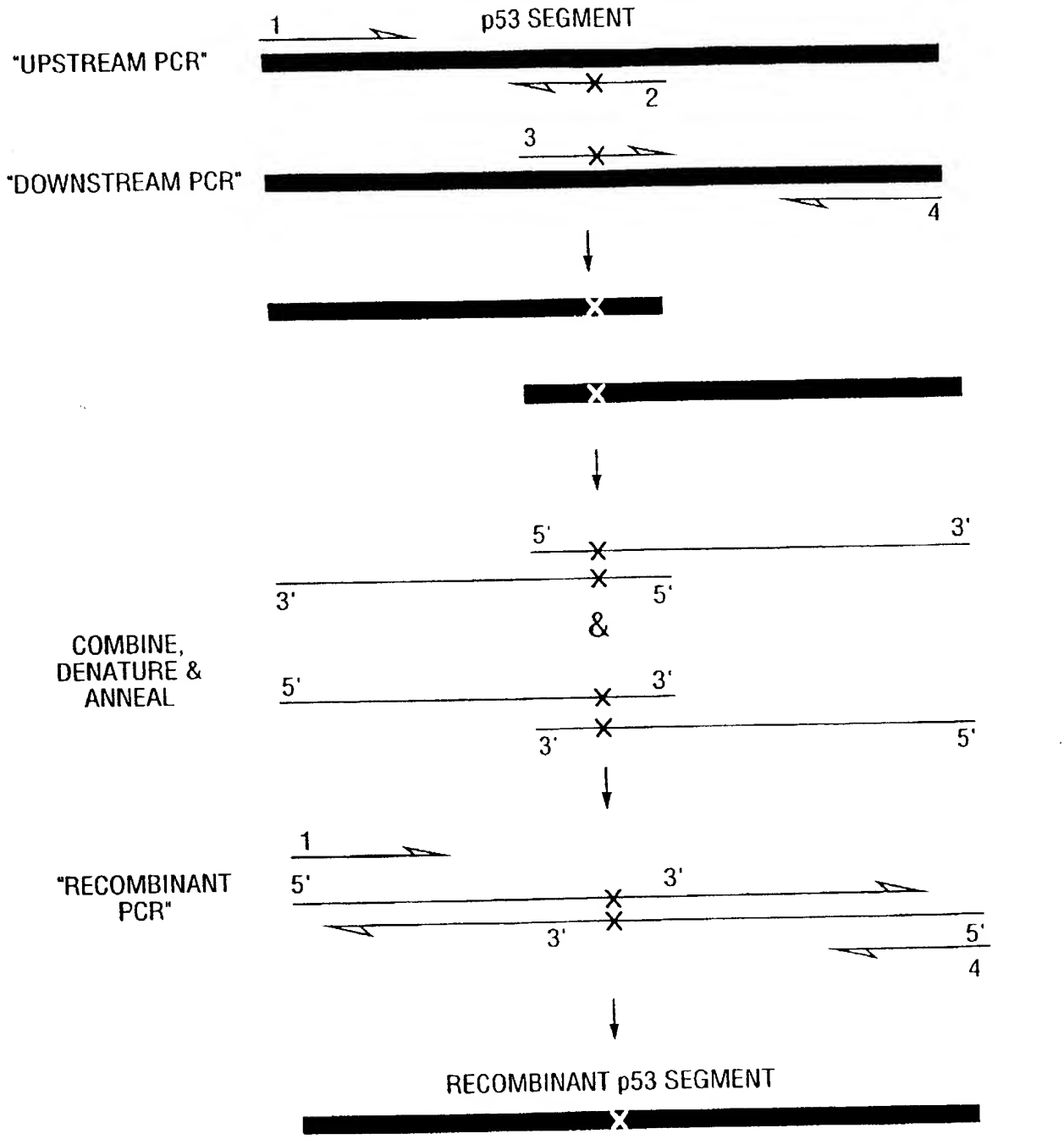

p53 SEGMENT
1
"UPSTREAM PCR"
2
3
"DOWNSTREAM PCR"
4
5'
3'
3'
5'
&
COMBINE, DENATURE & ANNEAL
5'
3'
3'
5'
1
"RECOMBINANT PCR"
5'
3'
3'
5'
4
RECOMBINANT p53 SEGMENT

FIG. 78

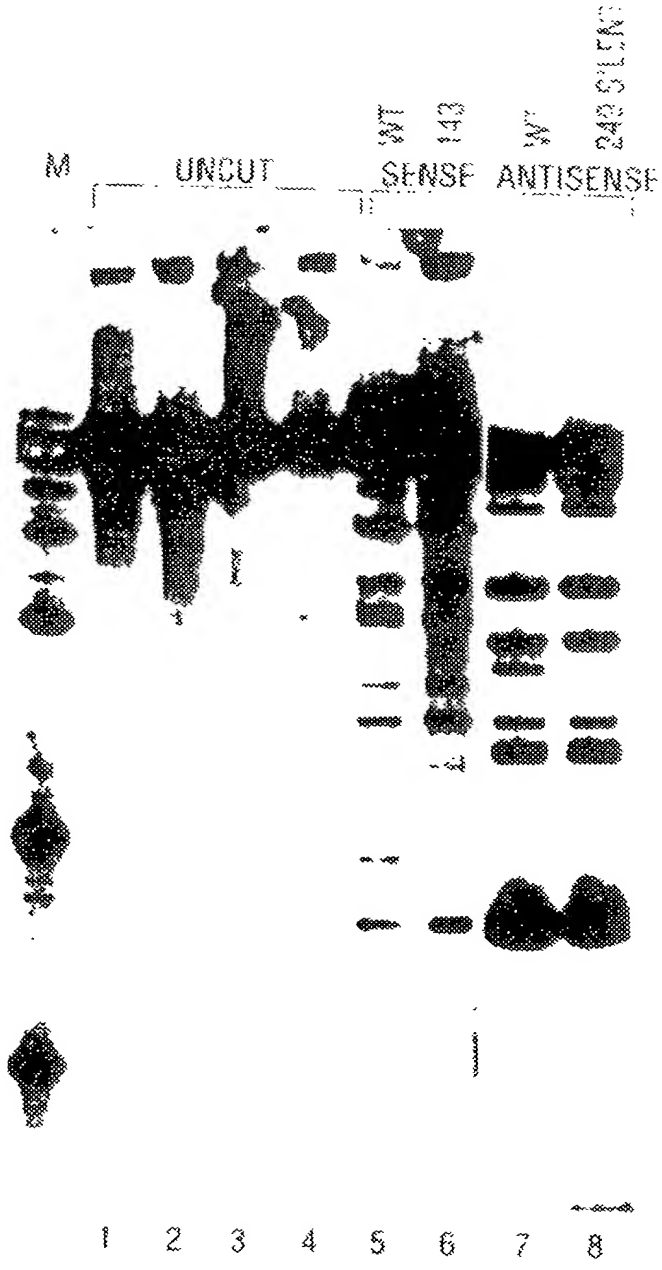


FIG. 79

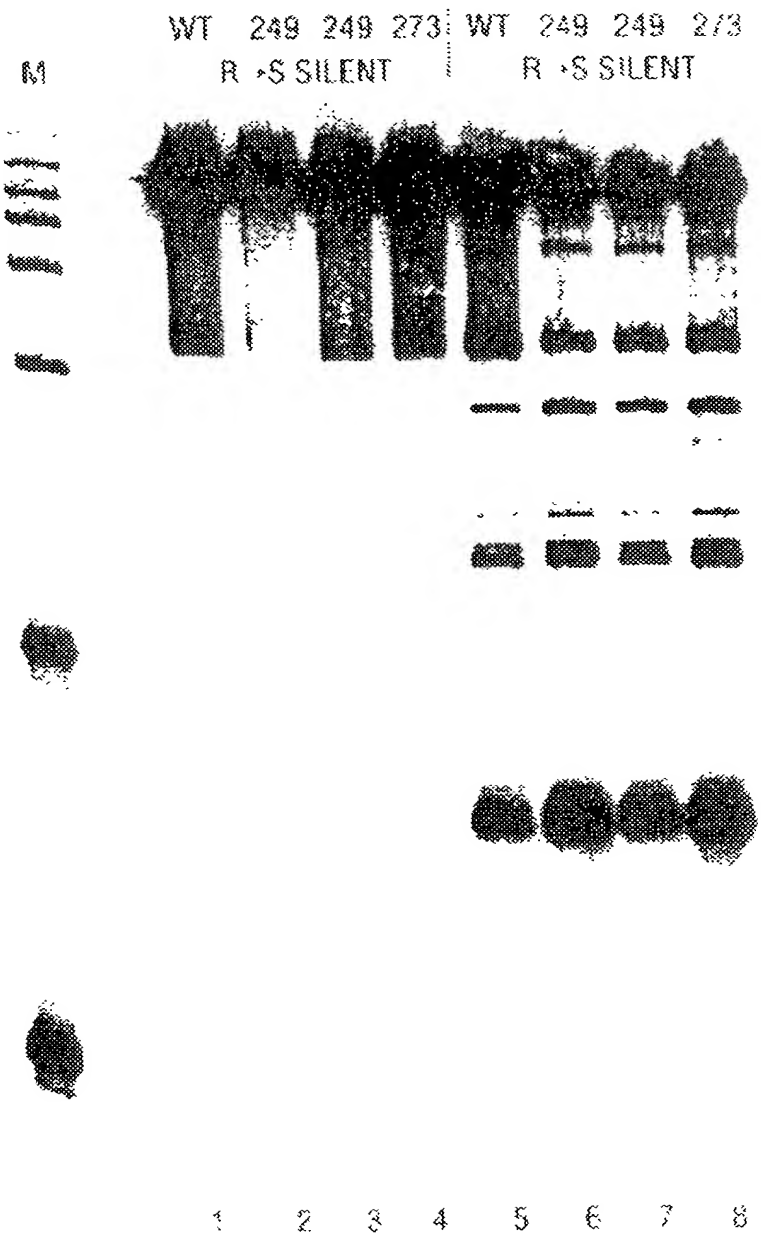


FIG. 80

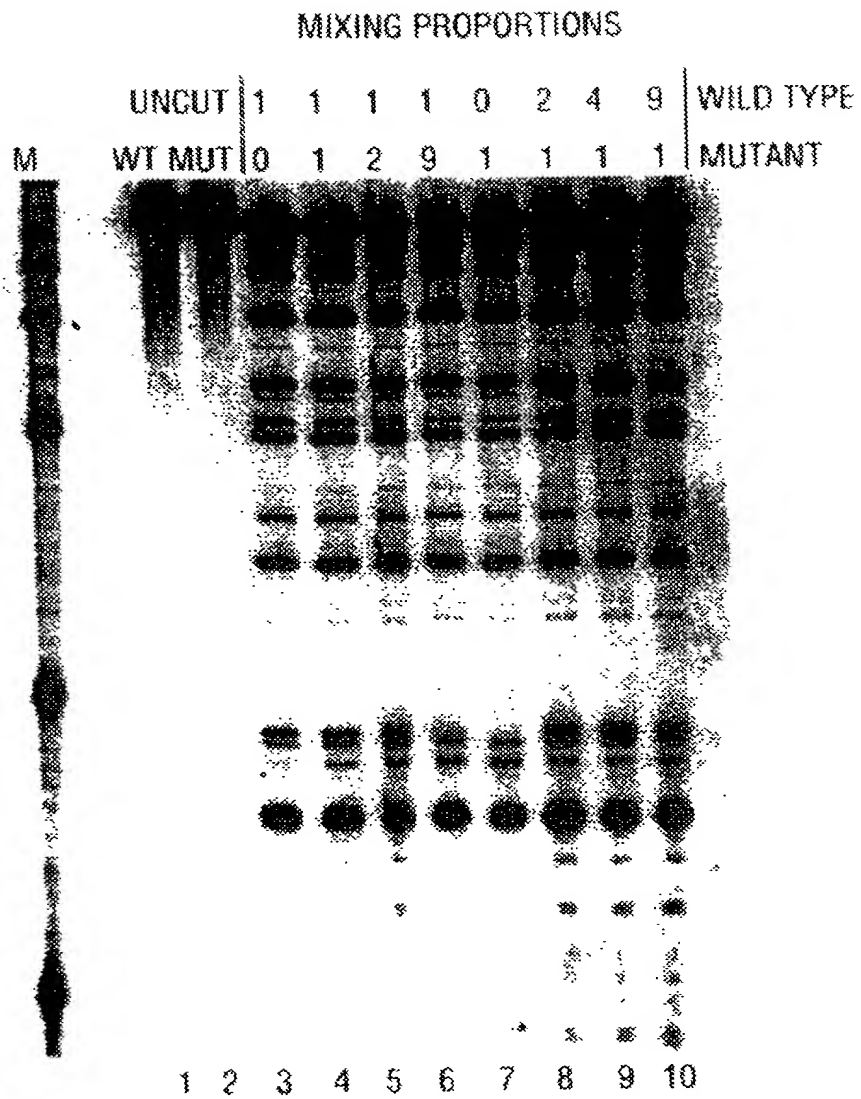

MIXING PROPORTIONS
UNCUT
WT MUT
M
1 1 1 1 0 2 4 9
0 1 2 9 1 1 1 1
WILD TYPE
MUTANT
1 2 3 4 5 6 7 8 9 10

FIG. 81

```
HCVI.1 (SEQ ID NO:121)    1 CTGTCTTCAC GCAGAAAGCG TCTGGCCATG GCGTTAGTAT GAGTGTCGTG 50
HCV2.1 (SEQ ID NO:122)      CTGTCTTCAC GCAGAAAGCG TCTAGCCATG GCGTTAGTAT GAGTGTCGTG
HCV3.1 (SEQ ID NO:123)      CTGTCTTCAC GCAGAAAGCG TCTAGCCATG GCGTTAGTAT GAGTGTCGTG
HCV4.2 (SEQ ID NO:124)      CTGTCTTCAC GCAGAAAGCG TCTAGCCATG GCGTTAGTAT GAGTGTCGTG
HCV6.1 (SEQ ID NO:125)      CTGTCTTCAC GCAGAAAGCG TCTAGCCATG GCGTTAGTAT GAGTGTCGTA
HCV7.1 (SEQ ID NO:126)      CTGTCTTCAC GCAGAAAGCG CCTAGCCATG GCGTTAGTAC GAGTGTCGTG

HCV1.1                     51 CAGCCTCCAG GACCCCCCCT CCCGGGAGAG CCATAGTGGT CTGCGGAACC 100
HCV2.1                        CAGCCTCCAG GACCCCCCCT CCCGGGAGAG CCATAGTGGT CTGCGGAACC
HCV3.1                        CAGCCTCCAG GICCCCCCCT CCCGGGAGAG CCATAGTGGT CTGCGGAACC
HCV4.2                        CAGCCTCCAG GACCCCCCCT CCCGGGAGAG CCATAGTGGT CTGCGGAACC
HCV6.1                        CAGCCTCCAG GCCCCCCCCT CCCGGGAGAG CCATAGTGGT CTGCGGAACC
HCV7.1                        CAGCCTCCAG GACCCCCCCT CCCGGGAGAG CCATAGTGGT CTGCGGAACC

HCV1.1                    101 GGTGAGTACA CCGGAATTGC CAGGACGACC GGGTCCTTTC TTGGAT-AAA 150
HCV2.1                        GGTGAGTACA CCGGAATTGC CAGGACGACC GGGTCCTTTC TTGGAT-CAA
HCV3.1                        GGTGAGTACA CCGGAATTGC CAGGACGACC GGGTCCTTTC TTGGAT-CAA
HCV4.2                        GGTGAGTACA CCGGAATTGC CAGGACGACC GGGTCCTTTC GTGGATGTAA
HCV6.1                        GGTGAGTACA CCGGAATTGC CGGGAAGACT GGGTCCTTTC TTGGAT-AAA
HCV7.1                        GGTGAGTACA CCGGAATCGC TGGGGTGACC GGGTCCTTTC TTGGAG-CAA
```

FIG. 82A

```
HCV1.1          151 CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCAAGA CTGCTAGCCG 200
HCV2.1              CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCAAGA CTGCTAGCCG
HCV3.1              CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCGAGA CTGCTAGCCG
HCV4.2              CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCCGCAAGA CTGCTAGCCG
HCV6.1              CCCACTCTAT GCCCGGCCAT TTGGGCGTGC CCCCGCAAGA CTGCTAGCCG
HCV7.1              CCCGCTCAAT ACCCAGAAAT TTGGGCGTGC CCCCGCGAGA TCACTAGCCG

HCVI.1          201 AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCCT 250
HCV2.1              AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT
HCV3.1              AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT
HCV4.2              AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT
HCV6.1              AGTAGCGTTG GGTIGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT
HCV7.1              AGTAGTGTTG GGTCGCGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT

HCVI.1          251 GCGAGTGCCC CGGGAGGTCT CGTAGACCGT GC 282
HCV2.1              GCGAGTGCCC CGGGAGGTCT CGTAGACCGT GC
HCV3.1              GCGAGTGCCC CGGGAGGTCT CGTAGACCGT GC
HCV4.2              GCGAGTGCCC CGGGAGGTCT CGTAGACCGT GC
HCV6.1              GCGAGTACCC CGGGAGGTCT CGTAGACCGT GC
HCV7.1              GCGAGTGCCC CGGGAGGTCT CGTAGACCGT GC
```

FIG. 82B

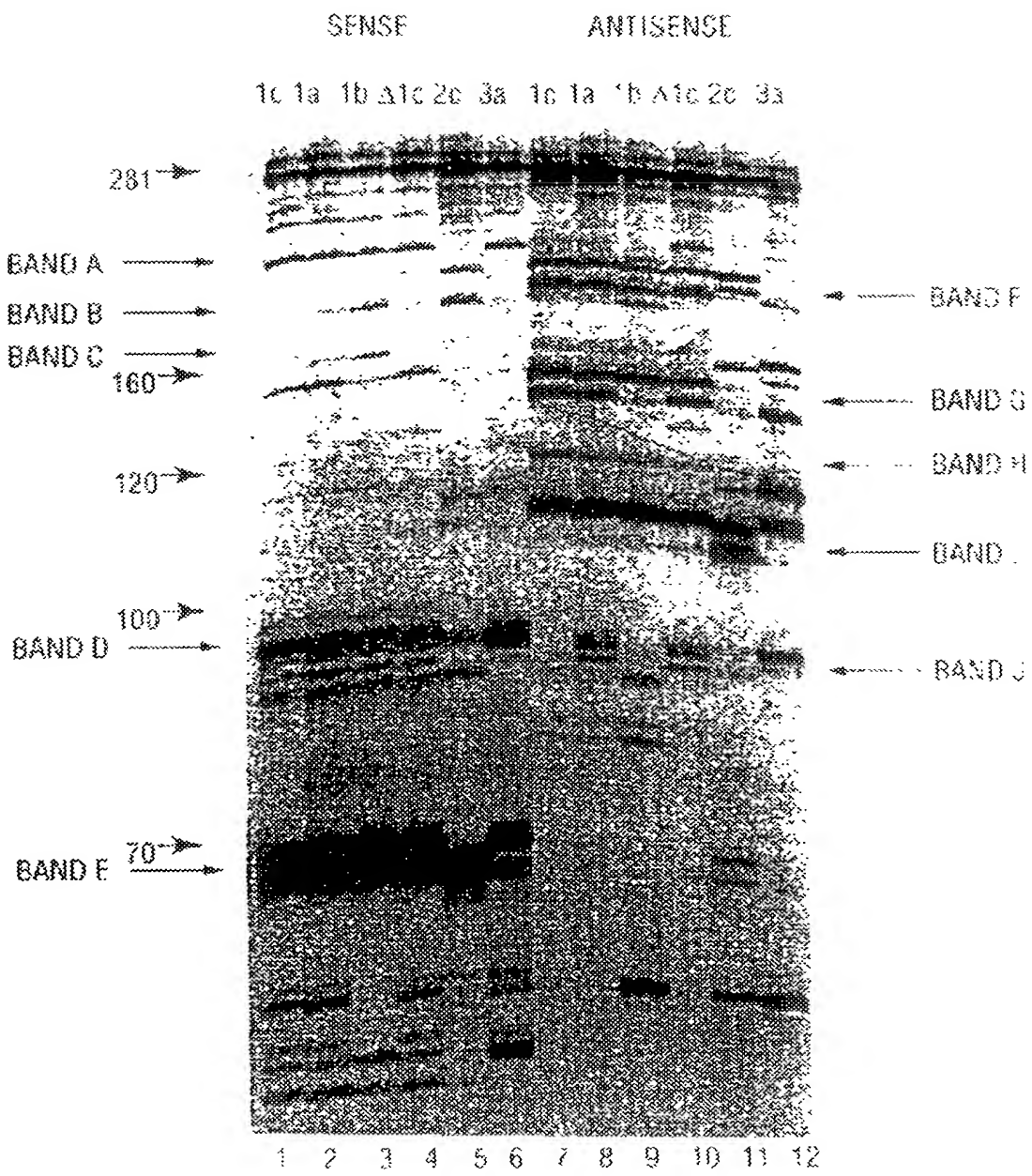

SENSE
ANTISENSE
1c 1a 1b Δ1c 2c 3a 1c 1a 1b Δ1c 2c 3a
281
BAND A
BAND B
BAND C
160
120
100
BAND D
70
BAND E
BAND F
BAND G
BAND H
BAND I
BAND J
1 2 3 4 5 6 7 8 9 10 11 12

FIG. 83

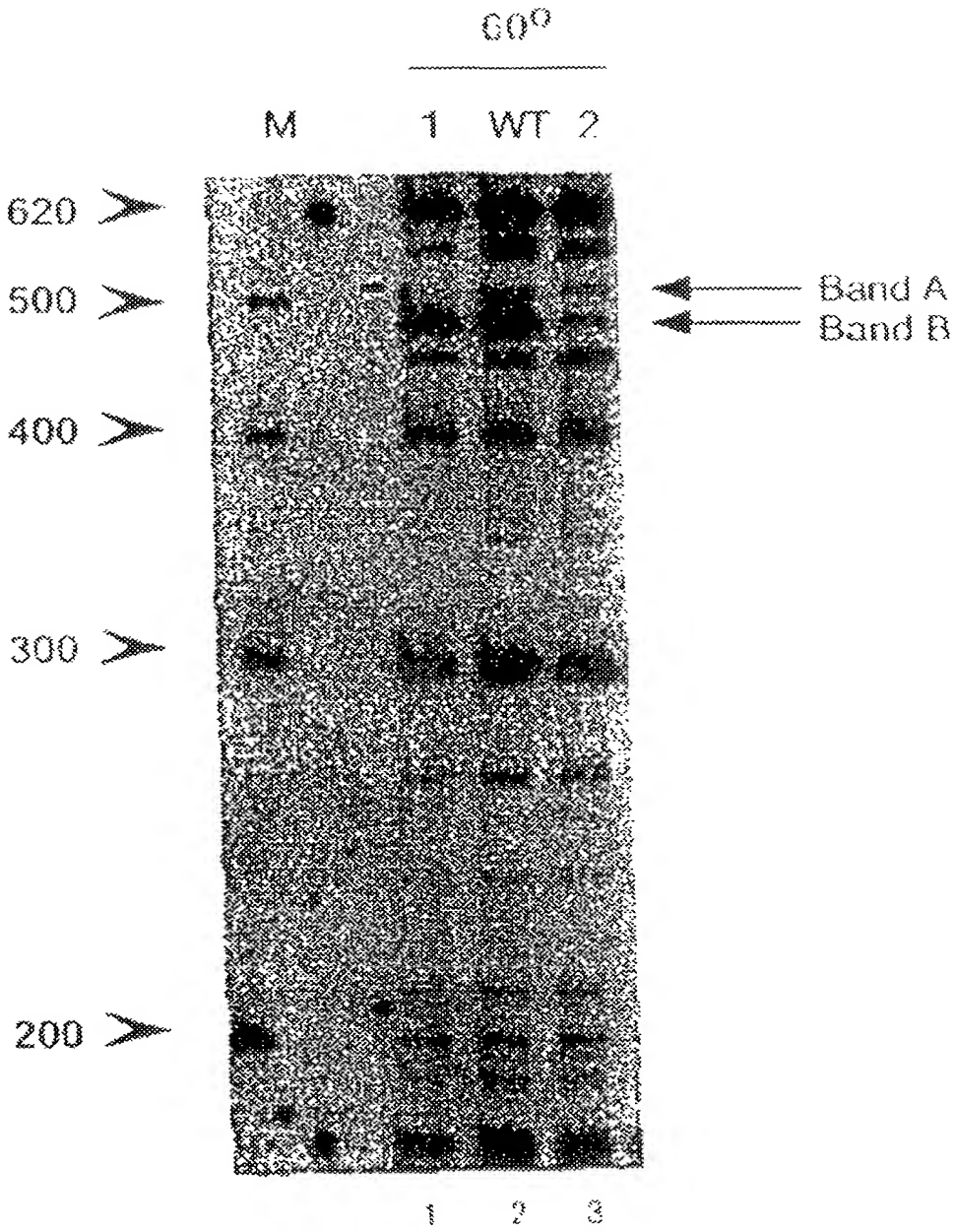


FIG. 84

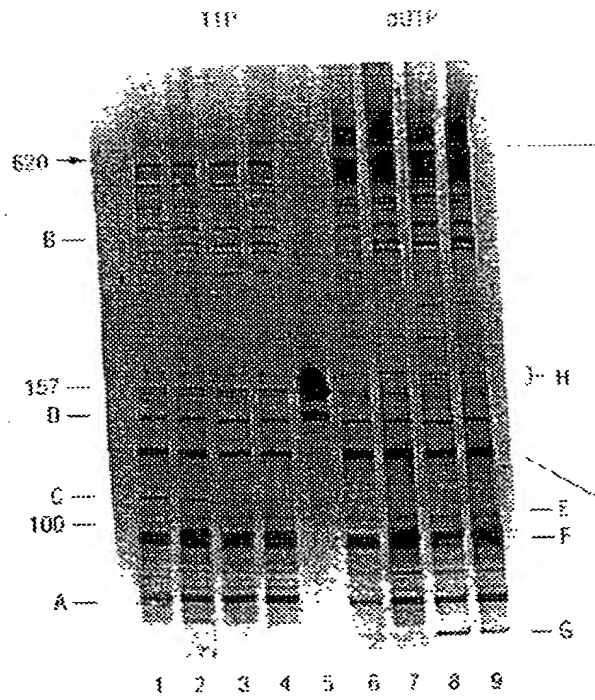


FIG. 85A

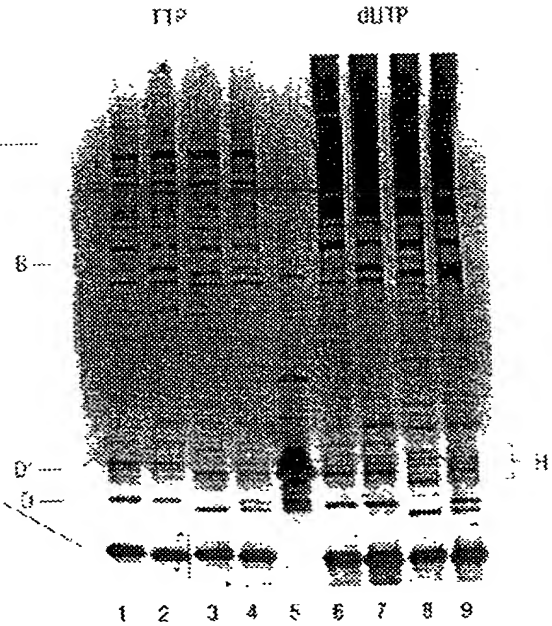


FIG. 85B

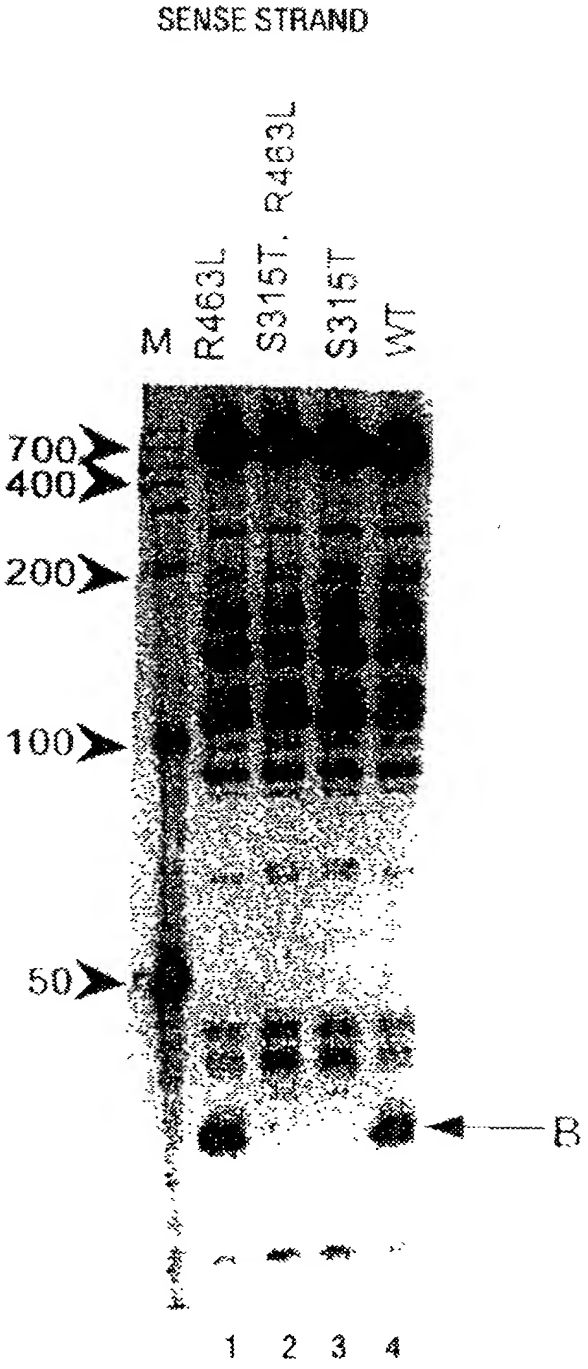

SENSE STRAND
M
R463L
S315T, R463L
S315T
WT
700
400
200
100
50
B
1
2
3
4

FIG. 86

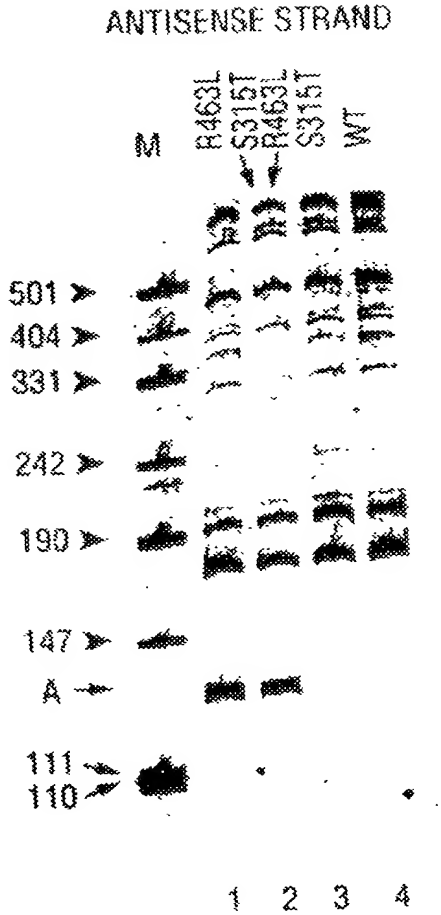

ANTISENSE STRAND
M
R463L
S315T
R463L
S315T
WT
501
404
331
242
190
147
A
111
110
1
2
3
4

FIG. 87

```
        10         20         30         40         50         60
       AGA GTTTGATCCT GGCTCAG                                        1638
AAATTGAAGA GTTTGATCAT GGCTCAGATT GAACGCTGGC GGCAGGCCTA ACACATGCAA
TTTAACTTCT CAAACTAGTA CCGAGTCTAA CTTGCGACCG CCGTCCGGAT TGTGTACGTT

        70         80         90        100        110        120
                                                GGCGGAC GGGTGAGTAA  ER10
GTCGAACGGT AACAGGAAGA AGCTTGCTTC TTTGCTGACG AGTGGCGGAC GGGTGAGTAA
CAGCTTGCCA TTGTCCTTCT TCGAACGAAG AAACGACTGC TCACCGCCTG CCCACTCATT

       130        140        150        160        170        180
TGTCTGGGAA ACTGCCTGAT GGAGGGGGAT AACTACTGGA AACGGTAGCT AATACCGCAT
ACAGACCCTT TGACGGACTA CCTCCCCCTA TTGATGACCT TTGCCATCGA TTATGGCGTA

       190        200        210        220        230        240
AACGTCGCAA GACCAAAGAG GGGGACCTTC GGGCCTCTTG CCATCGGATG TGCCCAGATG
TTGCAGCGTT CTGGTTTCTC CCCCTGGAAG CCCGGAGAAC GGTAGCCTAC ACGGGTCTAC

       250        260        270        280        290        300
GGATTAGCTA GTAGGTGGGG TAACGGCTCA CCTAGGCGAC GATCCCTAGC TGGTCTGAGA
CCTAATCGAT CATCCACCCC ATTGCCGAGT GGATCCGCTG CTAGGGATCG ACCAGACTCT

       310        320        330        340        350        360
GGATGACCAG CCACACTGGA ACTGAGACAC GGTCCAGACT CCTACGGGAG GCAGCAGTGG
CCTACTGGTC GGTGTGACCT TGACTCTGTG CCAGGTCTGA GGATGCCCTC CGTCGTCACC
                                    TGA GGATGCCCTC CGTCGTC          1659
```

FIG. 88A

```
        370         380         390         400         410         420
GGAATATTGC ACAATGGGCG CAAGCCTGAT GCAGCCATGC CGCGTGTATG AAGAAGGCCT
CCTTATAACG TGTTACCCGC GTTCGGACTA CGTCGGTACG GCGCACATAC TTCTTCCGGA

        430         440         450         460         470         480
TCGGGTTGTA AAGTACTTTC AGCGGGGAGG AAGGGAGTAA AGTTAATACC TTTGCTCATT
AGCCCAACAT TTCATGAAAG TCGCCCCTCC TTCCCTCATT TCAATTATGG AAACGAGTAA

        490         500         510         520         530         540
GACGTTACCC GCAGAAGAAG CACCGGCTAA CTCCGTGCCA GCAGCCGCGG TAATACGGAG
CTGCAATGGG CGTCTTCTTC GTGGCCGATT GAGGCACGGT CGTCGGCGCC ATTATGCCTC

        550         560         570         580         590         600
GGTGCAAGCG TTAATCGGAA TTACTGGGCG TAAAGCGCAC GCAGGCGGTT TGTTAAGTCA
CCACGTTCGC AATTAGCCTT AATGACCCGC ATTTCGCGTG CGTCCGCCAA ACAATTCAGT

        610         620         630         640         650         660
GATGTGAAAT CCCCGGGCTC AACCTGGGAA CTGCATCTGA TACTGGCAAG CTTGAGTCTC
CTACACTTTA GGGGCCCGAG TTGGACCCTT GACGTAGACT ATGACCGTTC GAACTCAGAG

        670         680         690         700         710         720
GTAGAGGGGG GTAGAATTCC AGGTGTAGCG GTGAAATGCG TAGAGATCTC GAGGAATACC
CATCTCCCCC CATCTTAAGG TCCACATCGC CACTTTACGC ATCTCTAGAC CTCCTTATGG

        730         740         750         760         770         780
GGTGGCGAAG GCGGCCCCCT GGACGAAGAC TGACGCTCAG GTGCGAAAGC GTGGGGAGCA
CCACCGCTTC CGCCGGGGGA CCTGCTTCTG ACTGCGAGTC CACGCTTTCG CACCCCTCGT
```

FIG. 88B

```
       790         800         810         820         830         840
AACAGGATTA GATACCCTGG TAGTCCACGC CGTAAACGAT GTCGACTTGG AGGTTGTGCC
TTGTCCTAAT CTATGGGACC ATCAGGTGCG GCATTTGCTA CAGCTGAACC TCCAACACGG

       850         860         870         880         890         900
CTTGAGGCGT GGCTTCCGGA GCTAACGCGT TAAGTCGACC GCCTGGGGAG TACGGCCGCA
GAACTCCGCA CCGAAGGCCT CGATTGCGCA ATTCAGCTGG CGGACCCCTC ATGCCGGCGT

       910         920         930         940         950         960
AGGTTAAAAC TCAAATGAAT TGACGGGGGC CCGCACAAGC GGTGGAGCAT GTGGTTTAAT
TCCAATTTTG AGTTTACTTA ACTGCCCCCG GGCGTGTTCG CCACCTCGTA CACCAAATTA

       970         980         990        1000        1010        1020
TCGATGCAAC GCGAAGAACC TTACCTGGTC TTGACATCCA CGGAAGTTTT CAGAGATGAG
AGCTACGTTG CGCTTCTTGG AATGGACCAG AACTGTAGGT GCCTTCAAAA GTCTCTACTC

      1030        1040        1050        1060        1070        1080
AATGTGCCTT CGGGAACCGT GAGACAGGTG CTGCATGGCT GTCGTCAGCT CGTGTTGTGA
TTACACGGAA GCCCTTGGCA CTCTGTCCAC GACGTACCGA CAGCAGTCGA GCACAACACT

      1090        1100        1110        1120        1130        1140
                    GC AACGAGCGCA ACCC                                    SB-1

AATGTTGGGT TAAGTCCCGC AACGAGCGCA ACCCTTATCC TTTGTTGCCA GCGGTCCGGC
TTACAACCCA ATTCAGGGCG TTGCTCGCGT TGGGAATAGG AAACAACGGT CGCCAGGCCG

      1150        1160        1170        1180        1190        1200
                                                    ATG ACGTCAAGTC    SB-3
                                                    ATG ACGTCAAGTC    SB-4

CGGGAACTCA AAGGAGACTG CCAGTGATAA ACTGGAGGAA GGTGGGGATG ACGTCAAGTC
GCCCTTGAGT TTCCTCTGAC GGTCACTATT TGACCTCCTT CCACCCCTAC TGCAGTTCAG
```

FIG. 88C

```
      1210        1220        1230        1240        1250        1260
ATCATGGCCC TTA                                                          SB-3
ATCATGGCCC TTACGA                                                       SB-4
ATCATGGCCC TTACGACCAG GGCTACACAC GTGCTACAAT GGCGCATACA AAGAGAAGCG
TAGTACCGGG AATGCTGGTC CCGATGTGTG CACGATGTTA CCGCGTATGT TTCTCTTCGC

      1270        1280        1290        1300        1310        1320
ACCTCGCGAG AGCAAGCGGA CCTCATAAAG TGCGTCGTAG TCCGGATTGG AGTCTGCAAC
TGGAGCGCTC TCGTTCGCCT GGAGTATTTC ACGCAGCATC AGGCCTAACC TCAGACGTTG

      1330        1340        1350        1360        1370        1380
TCGACTCCAT GAAGTCGGAA TCGCTAGTAA TCGTGGATCA GAATGCCACG GTGAATACGT
AGCTGAGGTA CTTCAGCCTT AGCGATCATT AGCACCTAGT CTTACGGTGC CACTTATGCA
                                                GC CACTTATGCA           1743

      1390        1400        1410        1420        1430        1440
TCCCGGGCCT TGTACACACC GCCCGTCACA CCATGGGAGT GGGTTGCAAA AGAAGTAGGT
AGGGCCCGGA ACATGTGTGG CGGGCAGTGT GGTACCCTCA CCCAACGTTT TCTTCATCCA
                                                                        1743
AGGGCCCGGA ACATG

      1450        1460        1470        1480        1490        1500
AGCTTAACCT TCGGGAGGGC GCTTACCACT TTGTGATTCA TGACTGGGGT GAAGTCGTAA
TCGAATTGGA AGCCCTCCCG CGAATGGTGA AACACTAAGT ACTGACCCCA CTTCAGCATT

      1510        1520        1530        1540        1550
CAAGGTAACC GTAGGGGAAC CTGCGGTTGG ATCACCTCCT TA.......
GTTCCATTGG CATCCCCTTG GACGCCAACC TAGTGGAGGA AT.......
```

FIG. 88D

```
                                                    AGAGTTTGATCCTGGCTCAG
1638 (SEQ ID NO:151)
E.colirrsE(SEQ ID NO:158)0 ...AAATTGAAGAGTTTGATCATGGCTCAGATTGAACGCTGGCGGCAGGCCTAACACATGCA
Cam.jejun5(SEQ ID NO:159)0 ~TTTTTATGGAGAGTTTGATCCTGGCTCAGAGTGAACGCTGGCGGCGTGCCTAATACATGCA
Stp.aureus(SEQ ID NO:160)0 ..TTTTATGGAGAGTTTGATCCTGGCTCAGGATGAACGCTGGCGGCGTGCCTAATACATGCA

                                                                                GGCGGACGGG
ER10 (SEQ ID NO:152)
E.colirrsE                    60 AGTCGAACGGTAACAG----GAAGAAGCTTGCTTCTTT----GCTGACGAGTGGCGGACGGG
Cam.jejunS                    62 AGTCGAACGAT-----GAAGCTTCTAGCTTGCTAGAAGTGGA-----TTAGTGGCGCACGGG
Stp.aureus                    61 AGTCGAGCGAA-----CGGACGAGAAGCTTGCTTCTCTGATG----TT-AGCGGCGGACGGG

                                  TGAGTAA
ER10
E.colirrsE                   114 TGAGTAATGTCTGGGA-AACTGCCTGATGGAGGGGGATAACTACTGGAAACGGTAGCTAATA
Cam.jejun5                   114 TGAGTAAGGTATAGTTAATCTGCCCTACACAAGAGGACAACAGTTGGAAACGACTGCTAATA
Stp.aureus                   113 TGAGTAACACGTGGATAACCTACCTATAAGACTGGGATAACTTCGGGAAACCGGAGCTAATA

E.colirrsE                   175 CCGCATAAC-------GTCGCAAGAC--------CAAAGAGGGGGACCTTCG-GGCCTCTTG
Cam.jejun5                   176 CTCTATACTCCTGCTTAACACAAGTTGAGTAGG-GAAAG---------TTTTT-------CG
Stp.aureus                   175 CCGGATAATATTTTGAACCGCATGGTTCAAAAGTGAAAGACGGT----CTT----GCTGTCA

E.colirrsE                   221 CCATCGGATGTGCCCAGATGGGATTAGCTAGTAGGTGGGGTAACGGCTCACCTAGGCGACGA
Cam.jejun5                   221 GTGTAGGATGAGACTATATAGTATCAGCTAGTTGGTAAGGTAATGGCTTACCAAGGCTATGA
Stp.aureus                   229 CTTATAGATGGATCCGCGCTGCATTAGCTAGTTGGTAAGGTAACGGCTTACCAAGGCAACGA

E.colirrsE                   283 TCCCTAGCTGGTCTGAGAGGATGACCAGCCACACTGGAACTGAGACACGGTCCAGACTCCTA
Cam.jejun5                   283 CGCTTAACTGGTCTGAGAGGATGATCAGTCACACTGGAACTGAGACACGGTCCAGACTCCTA
Stp.aureus                   291 TACGTAGCCGACCTGAGAGGGTGATCGGCCACACTGGAACTGAGACACGGTCCAGACTCCTA
1659(COMPL)                                                                     ACTCCTA
```

FIG. 89A


E.colirrsE 345 CGGGAGGCAGCAGTGGGGAATATTGCACAATGGGCGCAAGCCTGATGCAGCCATGCCGCGTG
Cam.jejun5 345 CGGGAGGCAGCAGTAGGGAATATTGCGCAATGGGGGAAACCCTGACGCAGCAACGCCGCGTG
Stp.aureus 353 CGGGAGGCAGCAGTAGGGAATCTTCCGCAATGGGCGAAAGCCTGACGGAGCAACGCCGCGTG
1659(COMPL) CGGGAGGCAGCAG
E.colirrsE 407 TATGAAGAAGGCCTTCGGGTTGTAAAGTACTTTCAGCGGGGAGGAA-GGGAGTAAAGTTAAT
Cam.jejun5 407 GAGGATGACACTTTTCGGAGCGTAAACTCCTTTTCTTAGGGAAG ----------AATT
Stp.aureus 415 AGTGATGAAGGTCTTCGGATCGTAAAACTCTGTTATTAGGGAAGAACATATGTGTAAGTAAC
E.colirrsE 468 ACCTTTGCTCATTGACGTTACCCGCAGAAGAAGCACCGGCTAACTCCGTGCCAGCAGCCGCG
Cam.jejun5 455 C----------TGACGGTACCTAAGGAATAAGCACCGGCTAACTCCGTGCCAGCAGCCGCG
Stp.aureus 476 -TGTGCACATCTTGACGGTACCTAATCAGAAAGCCACGGCTAACTACGTGCCAGCAGCCGCG

FIG. 89B

```
E.colirrsE   530 GTAATACGGAGGGTGCAAGCGTTAATCGGAATTACTGGGCGTAAAGCGCACGCAGGCGGTTT
Cam.jejun5   506 GTAATACGGAGGGTGCAAGCGTTACTCGGAATCACTGGGCGTAAAGGGCGCGTAGGCGGATT
Stp.aureus   538 GTAATACGTAGGTGGCAAGCGTTATCCGGAATTATTGGGCGTAAAGCGCGCGTAGGCGGTTT

E.colirrsE   592 GTTAAGTCAGATGTGAAATCCCCGGGCTCAACCTGGGAACTGCATCTGATACTGGCAAGCTT
Cam.jejun5   568 ATCAAGTCTCTTGTGAAATCTAATGGCTTAACCATTAAACTGCTTGGGAAACTGATAGTCTA
Stp.aureus   600 TTTAAGTCTGATGTGAAAGCCCACGGCTCAACCGTGGAGGGTCATTGGAAACTGGAAAACTT

E.colirrsE   654 GAGTCTCGTAGAGGGGGGTAGAATTCCAGGTGTAGCGGTGAAATGCGTAGAGATCTGGAGGA
Cam.jejun5   630 GAGTGAGGGAGAGGCAGATGGAATTGGTGGTGTAGGGGTAAAATCCGTAGATATCACCAAGA
Stp-aureus   662 GAGTGCAGAAGAGGAAAGTGGAATTCCATGTGTAGCGGTGAAATGCGCAGAGATATGGAGGA

E.colirrsE   716 ATACCGGTGGCGAAGGCGGCCCCCTGGACGAAGACTGACGCTCAGGTGCGAAAGCGTGGGGA
Cam.jejun5   692 ATACCCATTGCGAAGGCGATCTGCTGGAACTCAACTGACGCTAAGGCGCGAAAGCGTGGGGA
Stp.aureus   724 ACACCAGTGGCGAAGGCGACTTTCTGGTCTGTAACTGACGCTGATGTGCGAAAGCGTGGGGA

E.colirrsE   778 GCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGTCGACTTGGAGGTTGTGC
Cam.jejun5   754 GCAAACAGGATTAGATACCCTGGTAGTCCACGCCCTAAACGATGTACACTAGTTGTTGGGGT
Stp.aureus   786 TCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGAGTGCTAAGTGTTAGGGG
```

FIG. 89C

```
E.colirrsE   840 C-CTTGA-GGCGTGGCTTCCGGAGCTAACGCGTTAAGTCGACCGCCTGGGGAGTACGGCCGC
Cam.jejun5   816 G-CTAGT-CATCTCAGTAATGCAGCTAACGCATTAAGTGTACCGCCTGGGGAGTACGGTCGC
Stp.aureus   848 GT-TTCCGCCCCTTAGTGCTGCAGCTAACGCATTAAGCACTCCGCCTGGGGAGTACGACCGC

E.colirrsE   900 AAGGTTAAAACTCAAATGAATTGACGGGGGCCCGCACAAGCGGTGGAGCATGTGGTTTAATT
Cam.jejun5   876 AAGATTAAAACTCAAAGGAATAGACGGGGACCCGCACAAGCGGTGGAGCATGTGGTTTAATT
Stp.aureus   909 AAGGTTGAAACTCAAAGGAATTGACGGGGACCCGCACAAGCGGTGGAGCATGTGGTTTAATT

E.colirrsE   962 CGATGCAACGCGAAGAACCTTACCTGGTCTTGACATCCACGGAAGTTTTCAGAGATGAGAAT
Cam.jejun5   938 CGAAGATACGCGAAGAACCTTACCTGGGCTTGATATCCTAAGAACCTTTTAGAGATAAGAGG
Stp.aureus   971 CGAAGCAACGCGAAGAACCTTACCAAATCTTGACATCCTTTGACAACTCTAGAGATAGAGCC

E.colirrsE  1024 GTG--CCTTCGGG--AA-CCGTGAGACAGGTGCTGCATGGCTGTCGTCAGCTCGTGTTGTGA
Cam.jejun5  1000 GTGCTAGCTTGCTAGAA-CTTAGAGACAGGTGCTGCACGGCTGTCGTCAGCTCGTGTCGTGA
Stp.aureus  1033 TTCC-CCTTCGGG--GGACAAAGTGACAGGTGGTGCATGGTTGTCGTCAGCTCGTGTCGTGA

                                 GCAACGAGCGCAACCC
SB-1
E.colirrsE  1081 AATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCTTATCCTTTGTTGCCAGCGGTCCGG-CC
Cam.jejun5  1061 GATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCACGTATTTAGTTGCTAACGGTTCGG-CC
Stp.aureus  1092 GATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCTTAAGCTTAGTTGCCATCA-TTAAGT-T
```

FIG. 89D

```
                                                                                ATGACGTCAAGTCATC
SB-3 (SEQ ID NO:157)                                                            ATGACGTCAAGTCATC
SB-4 (SEQ ID NO:154)
E.colirrsE   1142 GGGAACTCAAAGGAGACTGCCAGTGATAAACTGGAGGAAGGTGGGGATGACGTCAAGTCATC
Cam.jejun5   1122 GAGCACTCTAAATAGACTGCCTTCG-TAAGGAGGAGGAAGGTGTGGACGACGTCAAGTCATC
Stp.aureus   1152 GGGCACTCTAAGTTGACTGCCGGTGACAAACCGGAGGAAGGTGGGGATGACGTCAAATCATC

SB-3                ATGGCCCTTA
SB-4                ATGGCCCTTACGA
E.colirrsE   1204 ATGGCCCTTACGACCAGGGCTACACACGTGCTACAATGGCGCATACAAAGAGAAGCGACCTC
Cam.jejun5   1183 ATGGCCCTTATGCCCAGGGCGACACACGTGCTACAATGGCATATAGAATGAGACGCAATACC
Stp.aureus   1214 ATGCCCCTTATGATTTGGGCTACACACGTGCTACAATGGACAATACAAAGGGCAGCGAAACC

E.colirrsE   1266 GCGAGAGCAAGCGGACCTCATAAAGTGCGTCGTAGTCCGGATTGGAGTCTGCAACTCGACTC
Cam.jejun5   1245 GCGAGGTGGAG-CAAATCTATAAAATATGTCCCAGTTCGGATTGTTCTCTGCAACTCGAGAG
Stp.aureus   1276 GCGAGGTCAAGCAAATCCCATAAAGTTGTTCTCAGTTCGGATTGTAGTCTGCAACTCGACTA

E.colirrsE   1328 CATGAAGTCGGAATCGCTAGTAATCGTGGATCAGA-ATGCCACGGTGAATACGTTCCCGGGC
Cam.jejun5   1306 CATGAAGCCGGAATCGCTAGTAATCGTAGATCAGCCATGCTACGGTGAATACGTTCCCGGGT
Stp.aureus   1338 CATGAAGCTGGAATCGCTAGTAATCGTAGATCAGC-ATGCTACGGTGAATACGTTCCCGGGT
                                                                      CGGTGAATACGTTCCCGGGC
1743(compl)
```

FIG. 89E

```
E.colirrsE   1389 CTTGTACACACCGCCCGTCACACCATGGGAGTGGGTTGCAAAAGAAGTAGGTAGCTTAACCT
Cam.jejun5   1368 CTTGTACTCACCGCCCGTCACACCATGGGAGTTGATTTCACTCGAAGCCGGAATACT--A-A
Stp.aureus   1399 ATTGTACACACCGCCCGTCACACCACGAGAGTTTGTAACACCCGAAGCCGGTGGAGTAACCT
1743(compl)       CTTGTAC

E.colirrsE   1451 TCG-GGAGGGCGCTTACCACTTTGTGATTCATGACTGGGGTGAAGTCGTAACAAGGTAACCG
Cam.jejun5   1427 AC---T-AGTTACCGTCCACAGTGGAATCAGCGACTGGGGTGAAGTCGTAACAAGGTAACCG
Stp.aureus   1461 TTTAGGAGCTAGCCGTCGAAGGTGGGACAAATGATTGGGGTGAAGTCGTAACAAGGTAGCCG

E.colirrsE   1512 TAGGGGAACCTGCGGTTGGATCACCTCCTTA---
Cam.jejun5   1485 TAGGAGAACCTGCGGTTGGATCACCTCCT-----
Stp.aureus   1523 TATCGGAAGGTGCGGCTGGATCACCTCCTTTCT-
```

FIG. 89F

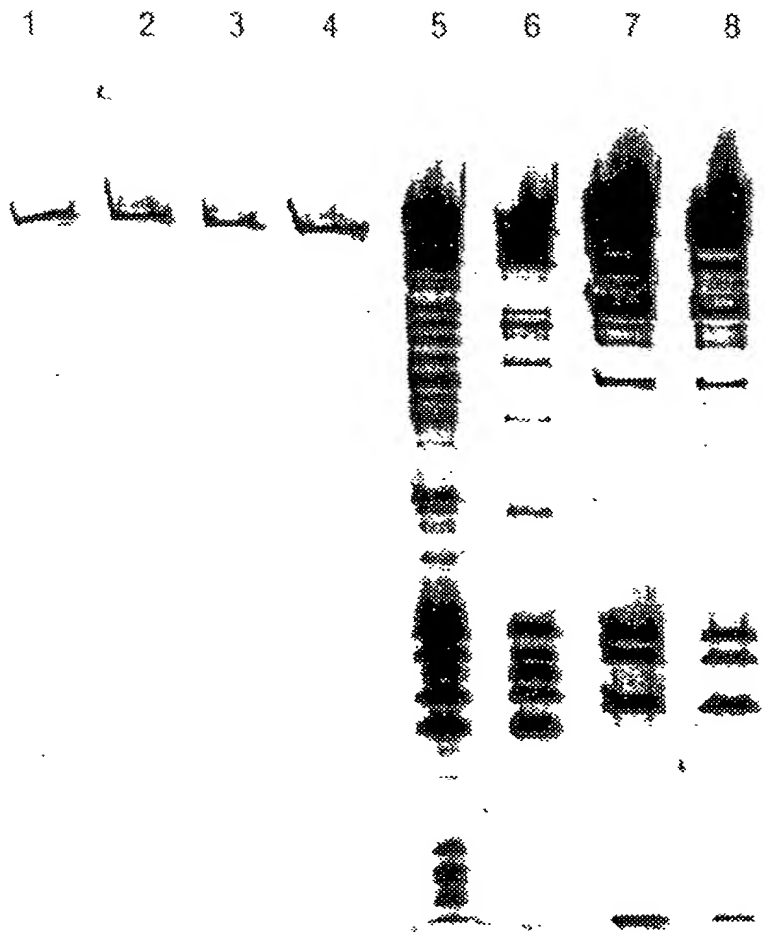


FIG. 90

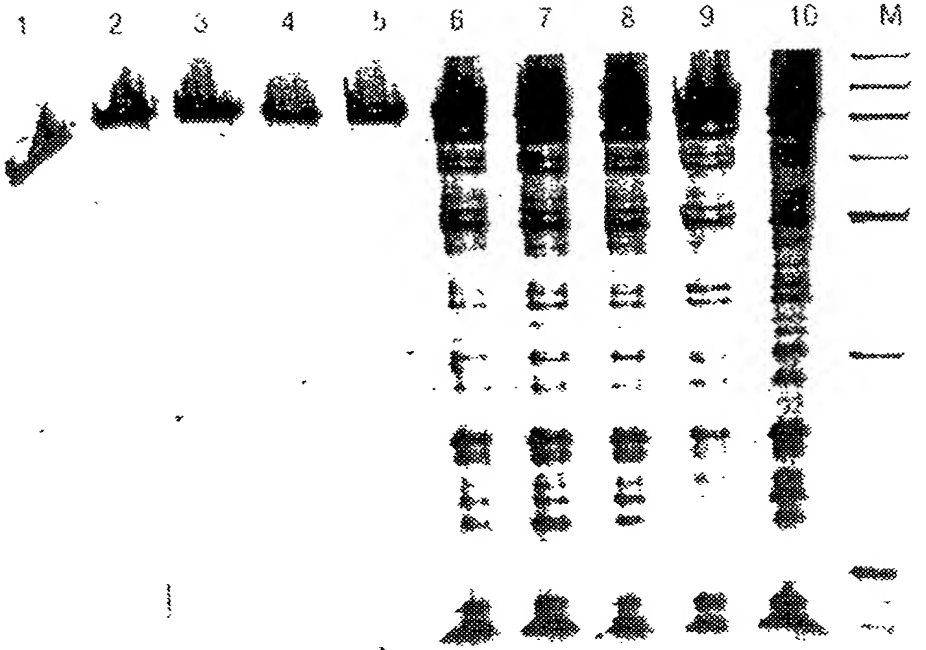


FIG. 91A

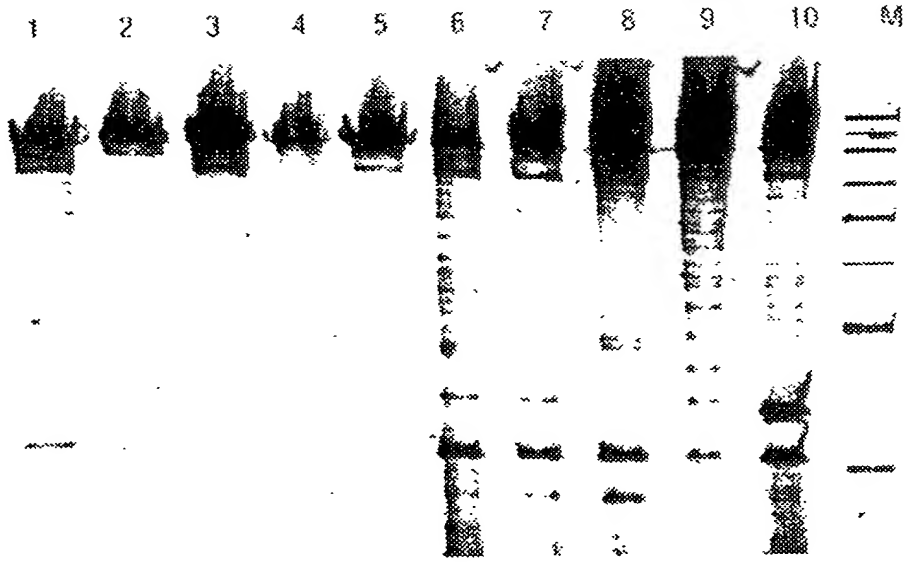


FIG. 91B

FIG. 92

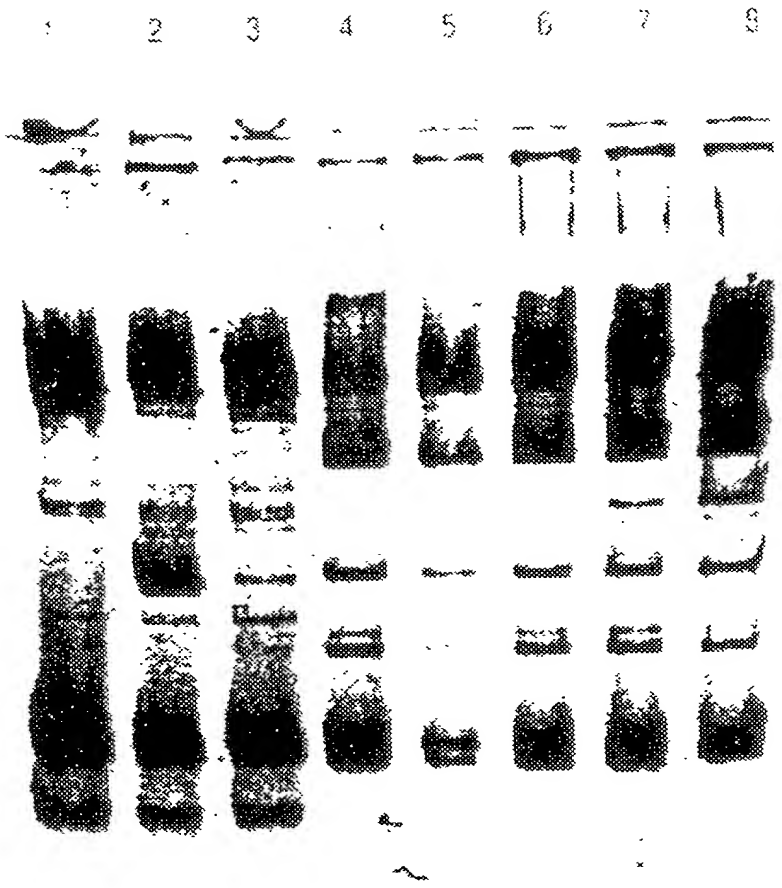


FIG. 93

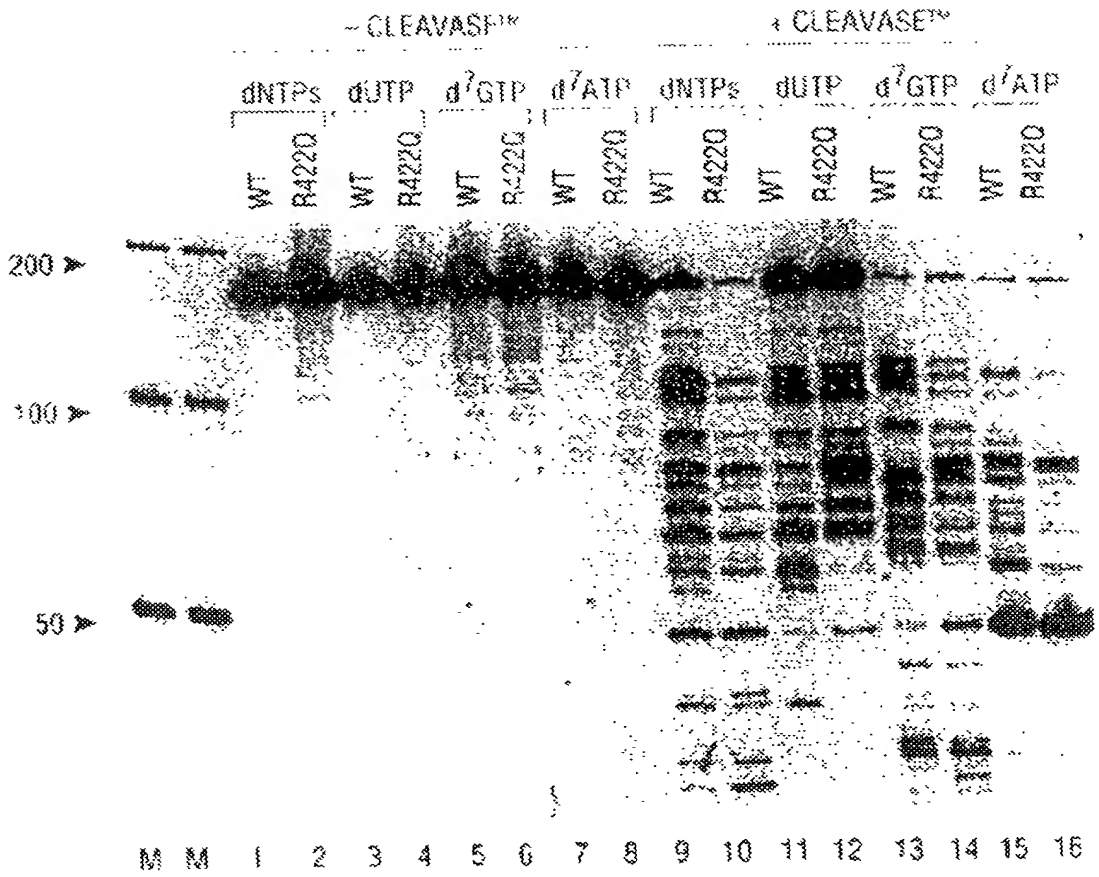

- CLEAVASE™
+ CLEAVASE™
dNTPs
dUTP
d7GTP
d7ATP
dNTPs
dUTP
d7GTP
d7ATP
WT
R422Q
200
100
50
M M 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

FIG. 94